G.F.TUCKER

Transactions

American Laryngological Association

SEVENTIETH VOLUME

"DOCENDO DISCIMUS"

TRANSACTIONS

OF THE

SEVENTIETH ANNUAL MEETING

OF THE

American Laryngological Association

1949

HELD AT THE BILTMORE

NEW YORK, N. Y.

MAY 16TH AND 17TH, 1949

PUBLISHED BY THE ASSOCIATION

ST. LOUIS, MO.

1949

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Top Row: P. A. Campbell, Lindsay, Schenck, Ashley, Theobald, H. L. Williams, Beck, Taylor, Johnston, Wishart, Cunning, Boies, Salinger, Hickey.

Third Row: Weille, C. L. Jackson, Holinger, Tucker, Van Alyea, New, Goodyear, Tobey, Lyman, Broyles, Canfield, Eagle, Morrison, Berry, Heatley, Woodward, Richards, Lukens.

Second Row: Hoople, Cody, Foster, White, Fenton, McMahon, McLaurin, Robb, Lillie, Grove, Maxwell, Engler, King, Schall, Goodale, Dixon.

Front Row: Proetz, Brown, Shurly, Coates, Hunt, Harkness, Orton, Hill, Hilding, Clerf, Mosher, Beatty, Imperatori, Shea, Ridpath, M. F. Jones, Havens.

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TRANSACTIONS OF THE SEVENTIETH ANNUAL MEETING

OF THE

American Laryngological Association

HELD AT

THE BILTMORE, NEW YORK, N. Y.

MAY 16TH AND 17TH, 1949

The Seventieth Annual Meeting of the American Laryngological Association was called to order by the President, Dr. Frederick T. Hill at The Biltmore, New York, N. Y.

REGISTRATION

The following Fellows were in attendance:

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BOIES, LAWRENCE R.
BOWERS, WESLEY C.
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ENGLER, CLARENCE W.
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Harkness, Gordon F.
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Heatley, Clyde A.
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Hilding, Anderson C.
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Hoople, Gordon D.
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Imperatori, Charles J.
Jackson, Chevalier L.
Jarvis, DeForest C.
Johnston, William H.
Jones, Marvin F.
Kelly, Joseph D.
King, Edward D.
Lierle, Dean M.
Lillie, Harold I.
Lindsay, John R.
Looper, Edward A.
Lukens, Robert M.
Lyman, Harry W.
Macpherson, Duncan
Maxwell, James H.
McCaskey, Carl H.
McLaurin, John G.
McMahon, Bernard J.
McNally, William J.
Morrison, William W.
Mosher, Harris P.
Nash, C. Stewart
New, Gordon B.
Orton, Henry B.
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Richards, Lyman G.
Ridpath, Robert F.
Robb, James M.
Salinger, Samuel
Schall, LeRoy A.
Schenck, Harry P.
Shea, John J.
Shurly, Burt R.
Taylor, H. Marshall
Theobald, Walter H.
Tobey, Harold G.
Tucker, Gabriel
Van Alyea, Oliver E.
Weille, Francis L.
White, Francis W.
Williams, Henry L.
Williams, Horace J.
Wishart, D. E. Staunton
Woodward, Fletcher D.

PRESIDENT'S ADDRESS

FREDERICK T. HILL, M.D.

WATERVILLE, ME.

I wish to express my sincere appreciation for the privilege of serving as your Chairman this past year, the 70th in the history of this society. No one could be unmindful of the great honor of being President of the American Laryngological Association.

The major portion of these remarks will be devoted to consideration of some of the broader applications of laryngology to the hospital and to other branches of medicine, to be followed by some thoughts as to the future of our specialty. Before taking up the main theme, certain references to the past would seem in order. The American Laryngological Association has a heritage of seventy years of distinguished service devoted to the advancement of laryngology. We are rightfully proud of this record and the accomplishments of these men of earlier days who are responsible for it. And so we endeavor to preserve the traditions of these seventy years.

I don't mean a slavish adherence to the past with a disregard for progressive ideas. Rather do I refer to a deference to time-honored customs, to the ideals upon which our Association was founded and to a recognition of the contributions of our predecessors. Tradition of the right kind is a good thing to tie to, especially so in these days, when we see many of our philosophies threatened by various and sundry radicalisms, untested and unproven, and dangerous in their implications.

Medicine has been defined as an art with a scientific background. We must not forget that this background rests upon a foundation of the labors and experiences of years of scientific study. While incidence may change and characteristics may vary, there are no new diseases other than those which are man-made. Many of our accomplishments which we hail as great discoveries either have been achieved before, perhaps less efficiently but under greater handicaps, or have

developed upon the basis of past work, often-times forgotten. Each generation has its torch-bearers and the brilliance of illumination varies only with the perspective.

Some time ago, I became interested in certain phases of hospital administration. This was an educational experience. I learned how little I knew about many things I previously had taken for granted. It was a natural step from this into active participation in the work of state and national hospital associations, something I never have regretted. I came to know what fine, unselfish, altruistic people there were in the hospital field. I feel that I gained a better and broader conception of this problem of caring for the sick. It is perhaps only natural that the clinician, concerned only with his own patient, so often fails to appreciate what is entailed in an adequate program of hospital care for that patient. He gives little thought to the financial problem of providing the stand-by service of building and equipment, of personnel, and of maintenance. At times he may give the impression that the hospital is dependent upon him, little realizing that without the hospital he would be quite unable to practice anything else than the most rudimentary medicine. Not only is the hospital of today a big business with all that this term implies; it must efficiently co-ordinate all professional services in order to maintain the highest standards, safeguarding the interests, the health and often the life of the patient.

One might compare the hospital to a symphony orchestra. In the orchestra, in order to effect a satisfactory performance, each member must play in harmony and in time under the conductor's baton. Doctors are natural soloists; specialists, notoriously so. And while the surgeon may solo in certain operating-room passages and the obstetrician may strike high C and perhaps sharp it a bit in the delivery-room, all must play together in tutti measures under the administrators' leadership. Otherwise there are bound to be discords, disastrous to both the patient and physician.

There is hardly a hospital program which does not devote considerable time to discussions of staff problems. It seems unfortunate that so often the physician is considered the problem child of the hospital family, and this is probably due to mutual lack of understanding. During the three years I served as President of my State

Hospital Association, I earnestly endeavored to interest all staff members, as well as trustees, in becoming members of the Association and in taking active part in its proceedings. A better understanding of hospital problems by all concerned, doctors and trustees, could not help but make for better standards of professional service.

Dr. Mosher repeatedly has urged that one be bigger than his specialty. To me, this means having the broadest possible conception of the practice of medicine, while confining one's actual work to that field in which one is trained and is considered competent. It might be phrased as being diagnostically broad and therapeutically limited. This requires constant association with men in other fields of medicine, thinking of the patient as a whole rather than any limited anatomical part thereof. It means group practice in the best professional sense, the pooling of all skills necessary for an adequate conception of any clinical problem. Unfortunately, most discussions of group practice have placed too much emphasis upon the economic phase, rather than on the more important objective of better medical service.

For years, the larger teaching hospitals have embodied the principles of group practice in the care of service cases. An outstanding feature in our changing professional relations in hospitals has been the gradual extension of this principle to all patients, private as well as service. It has been the logical thing to pool professional resources in the hospital. This should mean the group study of cases whenever indicated, the liberal use of consultations, and transferals to other services or physicians if the patient would benefit thereby.

Recently, I have been severely criticized, in the publication of one special society, for stating that the principle that the hospital should assume the responsibility for the safety and medical care of its patients is becoming gradually recognized. I stand by this statement, at least insofar as it refers to our best hospitals and most conscientious physicians. This does not mean that the hospital is attempting to practice medicine, but it does mean the members of its staff practicing it together. It means substituting co-operation for competition. It means a share of responsibility whenever indicated. It does not decry resourcefulness in meeting emergencies but it does eliminate attempting to play God when unnecessary.

It means that the private patient is not to be considered as the personal medical property of his physician, for him to do with as he may see fit. Rather, he is the hospital's patient, under the care of the physician, to be sure, but with the hospital, through its staff, being responsible for correct diagnosis and proper therapy. Medicine is not an exact science; no man is infallible and errors at times are bound to occur. The consensus of medical minds of the staff, by hospital policy, should be available to determine whether, or not, correct treatment is being carried out. The hallowed status of the physician who, under no circumstances should be criticized or interfered with in his relations with his private patients, still casts a shadow in many a hospital. And many a misdeed is perpetrated under the guise of ethics. Ethics is the science of morals and a hospital policy which does not consider the welfare of the patient as paramount would hardly seem to be truly ethical.

While this principle of the hospital assuming the responsibility through its staff for the medical care of its patients may seem revolutionary to some, it must be accepted if we are to assure the patient of the best possible care. And this, of course, is group practice in the hospital. And it is not new or revolutionary. This is simply the adaptation to all patients of the accepted principles of what we have termed the "teaching hospital," which has produced the best type of medicine the world has ever seen.

One might say that this is hardly a concern of this Association. We have been interested in the scientific advancement of laryngology. But, our members almost universally occupy senior positions as heads of departments, many of them in our leading institutions, and therefore should be able to exercise considerable influence in determining hospital policies. Perhaps unconsciously we have adopted the cloistered attitudes of the ivory tower and have given too little thought to the larger over-all problem of providing adequate care for the sick. The specialist is often the supreme example of the isolationist.

Medicine, as we have known it, is facing serious threats today. We hear criticisms of the cost of medical care and of the inability of many people to obtain adequate medical care. Actually, the most justifiable criticism is the cost of poor medical care, the toll of mistaken diagnoses, or diagnoses made too late, or the results of inadequate therapy. These, too often, produce costs that never can be

met, costs in lives sacrificed, or irreparably damaged. The promised panacea of political or government-controlled medicine would seem hardly the answer from all evidence at hand, yet it makes palatable political fodder.

Knowing that we have been doing our own particular job to the best of our ability, we have tended to remain aloof, satisfied that somehow a solution to this problem would be found. It is well to keep in mind that "nothing is so blind or insecure as the status quo."

The voluntary hospitals of the country, with the expansion planned for under the Hospital Survey and Construction Act, could provide hospital care and medical service of a standard to meet the demands of our people, and one comparable to that of our best institutions. They are desirous of providing this care but need the help and support of the best minds in the medical profession, such as are represented here today. Much could be accomplished by an active participation on our part in the work of our hospital associations. Should not we, specialists though we be, come down from our ivory tower? Should we not do all in our power to keep medicine free of politics?

In closing, I cannot refrain from some allusion to the changing character of our specialty. We hear criticisms that it represents a shrinking field; that antiobiotic and chemo- therapy have eliminated many of the demands for formerly common surgical procedures; that a better understanding of nasal physiology has lessened the frequency of much sinus surgery; that many facial plastic and endoscopic procedures are being lost to other specialties. The span of human life is far too brief to gain a true perspective of any era. Changes are inevitable; there always have been changes. And medicine, like life itself, is never static. I cannot agree that ours is a shrinking field; that our ambit is diminishing. There is nothing shrinking about it except possibly with our own mental processes. It is a changing specialty, just as medicine itself is changing, constantly changing. New discoveries gradually eliminate old procedures. New knowledge modifies older methods. And no single group has any monopoly on techniques, or should be dependent merely on technical ability.

This should mean that our horizons are broadened rather than narrowed. Any advance in medical knowledge which will lessen

morbidity or decrease mortality benefits all, both patients and physicians. Due to these developments we should be better able to devote more time and effort to the wider application of our specialty, and to become better physicians and less mere surgical technicians. To those of us who are hyphenates, practicing the twin specialty, the marked decrease in the incidence of surgical mastoiditis and its complications should allow for a more careful consideration of the many problems incident to hearing impairment, to prevention whenever possible, and to rehabilitation.

The recognition of nasal physiology and the consequent decrease in radical sinus surgery should allow time and stimulation for the study of underlying conditions, including a truly scientific approach to the problems of the allergic state, and to autonomic dysfunction. We blithely remove hypertrophic lymphoid tissue from the pharynx, but pay little attention to the possible causes of such hyperplasia. And while we seek an answer to the problem of cancer, many cases are still undiagnosed during the period when surgical removal would give a better prognosis and would result in less physical handicap to the patient. The salivary glands and their diseases, and infections and tumors of the neck have too long been accorded scanty attention, if not entirely neglected. These, as well as many other conditions, should be our responsibilty. We still have problems and there is abundant opportunity for work in our field, if we seek its widest application and explore it intensively.

PROFESSIONAL BUILDING.

FACTORS INFLUENCING THE GROWTH OF LYMPHOID TISSUE

ABRAHAM WHITE, PH.D.

LOS ANGELES, CALIF.

At the outset, may I express my appreciation and thanks for the invitation to address the American Laryngological Association. I suspect that this invitation is a result of my interest in the structure and function of lymphoid tissue. This interest apparently interdigitates with that of some members of this association, particularly in relation to the factors concerned with the size of lymphoid tissue. It is, therefore, my pleasant task to discuss with you some results obtained in studies of the regulation of lymphoid tissue growth. It should be made clear, however, at the beginining of this discussion that the data to be presented, obtained in the laboratories of other investigators, as well as our own, have been derived from experiments with laboratory animals. Nevertheless, it may perhaps be profitable for us to consider available information regarding the growth of lymphoid tissue in experimental animals, since it is from animal investigations that will stem observations which may have some practical application in man. Moreover, these applications will be made by members of this Association, and their colleagues, as a result of an evaluation of the significance of the experimental data against the background of clinical experiences.

The factors which affect the growth of lymphoid tissue may be listed in three broad categories: (1) diet, (2) endocrine secretions, and (3) stimuli other than hormonal, which may arise either within or outside of the organism. In addition, there are suggestions in the experimental literature that a genetic factor may modify the growth of lymphoid tissue.

Let us begin a consideration of the factors which influence the growth of lymphoid tissue by focusing our attention on the endocrine

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From the Department of Physiological Chemistry, School of Medicine, University of California, Los Angeles, California.

glands. The role of hormones in the regulation of lymphoid tissue size is discussed first since, as will be seen shortly, information available on this topic aids in explaining some of the effects of the other two factors, i.e., diet and nonhormonal stimuli, on lymphoid tissue.

Suggestion of a relationship between the size of lymphoid tissue and an endocrine gland, the adrenal cortex, was noted in the early descriptions of Addison's disease, in which hypertrophic changes in the lymphatic tissues were sometimes evident at autopsy. Within the last 20 years, numerous investigators have found that the secretions of the adrenal cortex may affect the size of the thymus gland. Injection of potent adrenal cortical extracts, or of certain adrenal cortical steroid hormones, resulted in involution of the thymus. On the other hand, experimental removal of the adrenal glands in animals led to lymphoid tissue hypertrophy.

It is well at this time to recall that the size and secretory rate of the adrenal cortex are under the control of the trophic hormone of the adenohypophysis, namely, adrenotrophin. In the animal from which the hypophysis has been removed by operation, there occurs an atrophy of the adrenal cortex, and a resultant inadequate production of its hormones. The restoration of the structure and function of the adrenal cortex of the hypophysectomized animal may be achieved by injection of either hypophyseal adrenotrophin, or hypophyseal extracts which have adrenotrophic hormone activity. Administration of excessive amounts of such preparations leads to manifestations of augmented adrenal cortical secretion, including lymphoid tissue involution. This is shown in data obtained in a study[1] of the effect of daily injections of adrenotrophin for 15 days into mice of the CBA strain (Strong). The reduction in lymphoid tissue size produced by chronic adrenal cortical stimulation may be contrasted with the lymphoid tissue hypertrophy occurring in circumstances of inadequate adrenal cortical secretion, as in the adrenalectomized animal.[1]

The marked decrease in size of lymphoid tissue induced by adrenal cortical hormones is based on profound histologic changes[2] in all tissues and organs containing lymphoid elements, e.g., thymus, lymph nodes, spleen and Peyer's patches. Within a few hours after a single injection of adrenotrophin, or of one of the adrenal cortical

steroids which is oxygenated in position 11 of the steroid nucleus, there is a dissolution of medium-sized and small lymphocytes within the lymphoid tissues. This is accompanied by a marked edema, and is characterized by karyorrhexis and pycnosis of the cells. There is also an increased development of immature plasma cells.

Dissolution of lymphocytes is maximal between one and six hours after hormone injection in both mice and rabbits. This is then followed by a development of numerous macrophages in all of the lymphoid organs. These macrophages contain large amounts of ingested material as a result of their phagocytic activity in removing the cellular debris arising from the dissolution of lymphocytes. The phagocytic reaction is not unlike that following a bacterial invasion or injection. Within six to nine hours after administration of either adrenotrophic or adrenal cortical hormones, most of the nuclear fragments scattered about in the lymphoid tissues have been phagocytized, and there is little evidence of further lymphocyte dissolution. During this period and subsequently, the edema has subsided and there is evident the beginning of a return to normal lymphoid structure. The period of recovery is characterized by differentiation of lymphocytes from reticulum cells and resumption of mitosis in lymphocytes. Within 24 hours after a single injection of hormone, the lymphoid structures, with the exception of the thymus, usually contain normal numbers of lymphocytes. This series of histologic events may be repeated following another injection of hormone, although small hyperplastic lymph nodes may result from prolonged hormonal administrations. It seems clear from the evidence presented that at least one endocrine gland, the adrenal cortex, controlled in its secretory rate by the adenohypophyseal adrenotrophic hormone, influences profoundly the size of lymphoid tissue.

The control exerted by hypophyseal adrenotrophin over the secretory rate of the adrenal cortex is of particular interest in evaluating the relation of this endocrine gland to the size of lymphoid tissue, since a wide variety of unrelated stimuli are now known to augment the rate of secretion of adrenotrophin.[3] Thus, exposure of the organism to environmental influences such as cold, heat, or anoxia, to traumatic conditions such as tissue injury, fractures or hemorrhage, to bacterial toxins, to toxic chemicals, e.g., arsenic or benzene, to anesthetics, e.g., nembutal, to foreign proteins, or to minute

amounts of a variety of substances normally produced in the organism, such as histamine, insulin, epinephrine and thyroxine, will produce an increased rate of secretion of hypophyseal adrenotrophin. As a consequence, there results an augmented production of adrenal cortical steroids and an accentuation of those processes which are influenced by these steroid hormones. The accelerated release of adrenal cortical hormones, as a result of any one of these stimuli, does not occur in the absence of the hypophyseal adrenotrophic hormone. These observations serve to explain why the various physiological alterations which are affected by pituitary-adrenal cortical secretion may be seen to a qualitatively similar extent in response to a wide variety of agents and in diverse circumstances. This endocrine mechanism is undoubtedly the physiological basis for the so-called "accidental involution" of lymphoid tissue, and for the decrease in lymphoid tissue size seen in the "alarm reaction" of Seyle,[4] inasmuch as stress, whether physical or chemical, is one of the potent activators of pituitary-adrenal cortical secretion. Thus, the fact that the histological and physiological responses of lymphoid tissue are so greatly influenced by a particular endocrine mechanism, the hypophyseal-adrenal cortical relationship, which in turn may be augmented by many stimuli, suggests a reason for the difficulty in finding uniformly, at biopsy or autopsy, a so-called normal appearance of lymphoid structures. It would appear that the latter are, literally, in a state of continuous histological and physiological flux in response to continual variations in the secretory rate of the pituitary-adrenal cortical mechanism. This rate is, in turn, influenced markedly by a variety of diverse stimuli which may have their origin either within the organism or in its environment.

It should be emphasized that stimuli operating independently of the pituitary-adrenal cortical mechanism may influence profoundly the size and structure of lymphoid tissue. This is evident from experience which shows that certain agents may cause lymphoid tissue involution in the absence of the hypophysis or the adrenals. For example, exposure to x-radiation, or injection of either a nitrogen mustard, urethane, or desoxypyridoxine, results in lymphoid tissue involution in the hypophysectomized or the adrenalectomized animal. Thus, a direct effect of any one of these agents on lymphoid tissue without endocrine mediation is well established. It may be pointed out, however, that in the intact animal, a portion of these effects

may be endocrine mediated, since these toxic agents do augment pituitary-adrenal cortical secretion.[5]

A striking example of the profound role which the pituitary-adrenal cortical mechanism may play in the normal organism, even in circumstances in which the stimulus can affect lymphoid tissue without endocrine mediation, is seen in the case of x-radiation. It has been established that x-radiation, in common with a variety of other types of stimuli, also augments pituitary-adrenal cortical secretion.[6, 7] However, it is also clear from the experimental data that while small doses of radiation may exert their effects on lymphoid tissue structure and function only by way of the pituitary-adrenal cortical mechanism, larger radiation doses produce alterations in lymphoid tissue either in the presence or absence of the pituitary or the adrenals. Indeed, x-radiation is one of the most useful methods of producing localized lymphoid tissue involution, since by careful shielding of all except the area which it is desired to radiate and with proper choice of dosage, the effects of the radiation can be largely restricted. However, attention should be directed to the fact that even in circumstances of extensive protection of most of the organism, there may be a generalized effect of radiation on lymphoid tissue via pituitary-adrenal activation. This is seen most strikingly in the experiments of Leblond and Seegal.[8] These investigators observed that exposure of only the posterior one-third of normal rats to x-rays caused generalized lymphoid tissue involution. However, very large radiation doses given to adrenalectomized animals, shielded in all but the thymic area, produced alterations only in the exposed thymic tissue. These experiments are an illustration of the fact that generalized lymphoid alterations, seen following exposure of a circumscribed area to x-radiation, may be endocrine mediated.

The experimental use of x-radiation has also provided further emphasis of the role which the adrenal cortical hormones play in the normal organism in restricting abnormal enlargement of lymphoid tissue. Mice given a single dose of 200 r show significantly smaller lymphoid structures, as compared to untreated mice, for as long as 48 to 72 hours following exposure. In contrast, adrenalectomized mice, given the same radiation dose, show extremely rapid restitution of lymphoid tissue. Within 24 hours following exposure of adrenalectomized mice to 200 r, the lymphoid tissue had not only regained

its normal size, but had attained the typically hyperplastic appearance characteristic of the adrenalectomized animal.[6] In other words, the rate of accumulation of lymphoid cells is enormously greater in the absence of the adrenals. On the other hand, since in intact animals exposed to single, high radiation doses, the lymphoid tissue is maintained in the involuted state for several days, there must be occurring a prolonged augmentation of pituitary-adrenal cortical secretory activity. Thus, although the lymphoid tissue involution was induced initially largely as a result of the direct action of x-radiation on lymphoid cells, the postradiation period is characterized by enhanced activity of the endocrine mechanism, with its attendant restriction of lymphoid tissue growth. These data illustrate the intimate relationships which may obtain between direct and indirect effects on lymphoid tissue, elicited by the same agent, for example, x-radiation.

In considering endocrine glands other than the adrenal cortex, which may be concerned with the regulation of the size of lymphoid tissue, perhaps the next best evidence can be assembled for a relationship between the sex glands and lymphoid tissue mass. The well known involution of lymphoid tissue, which occurs at puberty, is a long-established observation. For example, the involution of the palatine tonsils seems to begin about the age of 15. The thymus gland undergoes marked involution concomitant with the attainment of sexual maturity.

In the case of the estrogens, these steroid hormones appear to exert a two-fold influence on lymphoid tissue. Small doses of these hormones may increase the output of pituitary adrenotrophic hormone, and this can account for the typical involution of the thymus, which may be produced experimentally by the injection of estrogens. However, prolonged administration of the female sex hormones leads subsequently, in the thymus, to active growth of an epithelial nature. With respect to other lymphoid tissues, it has been demonstrated that chronic estrogen administration, either by injection of the hormone, implantation of pellets, or painting of the skin with estrogens, produces a local or general enlargement of lymph nodes and thymus gland, and that ultimately, provided the animal does not die from the effects of hormone overdosage, there may be produced lymphoid tumors.[9] A genetic factor appears to exert an important influence in this connection, inasmuch as some strains of highly inbred mice

are much more susceptible than others to the induction of lymphoid tumors by estrogens. It is interesting in this connection that the total amount of lymph nodes and splenic lymphatic tissue is generally greater in female than in male experimental animals. The sex difference is most pronounced, generally, for the thymus.

The male sex hormone, testosterone, also has been observed experimentally to exert a marked influence on the size of lymphoid tissue. Castration has been reported to cause a highly significant enlargement of lymphoid structures, while the injection of male sex hormone has caused involution of lymphoid structures. The influence of the gonads in the regulation of the size of lymphoid tissue is seen in recent observations in fasting, castrate mice.[10] The marked involution of lymphoid tissue occurring as a result of a stress, in these experiments inanition, was found to be reduced in severity by prior gonadectomy. Apparently, the castrate animal, when exposed to stress, does not respond with a normal degree of pituitary-adrenal cortical secretory activity.

As for the possible influence of other endocrine secretions on the growth of lymphoid tissue, at least two of these, namely, insulin and epinephrine, are known to augment pituitary-adrenal cortical secretion, and may, therefore, indirectly bring about an involution of lymphoid tissue. The active secretion of the thyroid, controlled by the thyrotrophic hormone of the adenohypophysis, may acutely cause reduction of lymphoid tissue size as a result of stimulation of adrenotrophin secretion. Chronically, however, thyroid secretion appears to stimulate the growth of lymphoid tissue, since enlarged lymphoid structures have been observed in experimental thyroid feeding and in clinical hyperthyroidism.

From the foregoing, it seems evident that a wide variety of endocrine influences may alter the size and structure of lymphoid tissues. The important role which these endocrine secretions play in the normal physiology of the organism, and the wide variety of factors which influences the concentration of these circulating hormones, all point to intimate relationships between endocrine glands and the size of lymphoid tissue.

Let us turn now to a consideration of the role of diet in the regulation of the size and structure of lymphoid tissue. At least two dietary factors have been demonstrated to affect the growth of

lymphoid structures. These are: (1) the caloric intake, and (2) the protein content of the diet. With regard to calories, it is obvious that growth, whether it be of the entire organism or of a specific tissue, i.e., lymphoid organs, is an energy-requiring phenomenon. Consequently, an adequate caloric intake is essential for the promotion of growth. In addition, it has now been established that caloric restriction exerts an effect on lymphoid tissue which is unique in its intimate relationship to pituitary-adrenal cortical secretion. One of the oldest of experimental observations is the marked involution of lymphoid tissue, which occurs as the result of partial or total inanition. Indeed, inanition has been used by histologists for many years for the purpose of producing involution of lymphoid tissue with the view of providing so-called "washed-out" or depleted lymphoid structures for histological examination by students. Since acute or chronic inanition has been shown to be a potent activator of pituitary-adrenal cortical secretion, it was considered possible, as a working hypothesis, that an increased concentration of circulating adrenal cortical steroids is the basis of the striking lymphoid tissue involution caused by acute or chronic inanition. Experiments designed to test this hypothesis have been conducted in fasting mice.[11] Normal mice of the CBA strain (Strong), subjected to a 48-hour fast, show a decrease of at least 35% in lymphoid tissue weight and nitrogen content, as compared to normal, fed animals. At the same time, there occurs the often-observed loss of weight and nitrogen from the liver and remainder of the body. On the other hand, adrenalectomized mice, fasted for a comparable period of time, show no loss of lymphoid tissue weight or nitrogen content, although decreases in the liver and other tissues of the body are seen, as in the non-operated, fasted mice. Therefore, in the absence of the adrenals, the fasting animal is unable to obtain readily the direly needed nitrogen present in its lymphoid tissue. It seems clear, therefore, that the total caloric intake is an exceedingly important factor regulating the size of lymphoid tissue, and that the involution of these structures, which occurs in circumstances of partial or complete restriction of food intake, is based upon the sensitivity of the pituitary-adrenal cortical secretory mechanism in its response to restricted caloric intake.

In connection with the described experiments in fasting mice, recent studies have been conducted on the influence of purified hypo-

physeal growth hormone on fasting metabolism.[12] The growth of lymphoid tissue, which is seen following adrenalectomy, occurs even in the fasting animal, notwithstanding the obvious drain on the energetic resources imposed by the fast. This growth of lymphoid tissue in the fasted, adrenalectomized animal could not be potentiated by growth hormone. Thus, the specific role of the adrenal in regulating the structure and function of lymphoid tissue gains emphasis from the failure to influence this tissue with growth hormone, which has, in general, a nitrogen-sparing effect in the fasting animal.

In addition to the caloric intake, it is clear that the protein content of the diet may be a prime factor in determining the size of lymphoid tissue. In the first place, in circumstances of an inadequate dietary content of protein, there is generally a diminution in appetite, and this partial inanition may, in itself, lead to lymphoid tissue involution via stimulation of the pituitary-adrenal cortical mechanism. Secondly, protein, per se, is required in order to provide the construction material necessary for the synthesis of the protoplasm of new lymphoid cells. Insofar as is known at the present time, the requirements of lymphoid tissue for protein are not unlike those of other structures, i.e., a minimum amount of protein nitrogen must be available in the diet, and the quality of the protein must be nutritionally adequate; that is to say, the so-called ten essential amino acids which cannot be synthesized readily by the organism must be available in the dietary protein. The role of protein in the synthesis of lymphoid tissue is seen specifically in the studies of Cannon and his associates[13, 14] at the University of Chicago. Using antibody production as an index of measuring the synthetic capacity of lymphoid tissue, these investigators demonstrated a diminished rate and degree of antibody synthesis in rabbits maintained on a restricted protein intake.

A further manifestation of the requirement of lymphoid tissue for protein or protein components may be seen in the recent demonstration[15, 16] that a severe atrophy of the thymus occurs in paired-fed rats given a synthetic diet lacking in either phenylalanine or leucine, two of the so-called essential amino acids. Moreover, attention should be directed to the experimental evidence[17] that restriction of a diet in its cystine content caused reduction of the incidence of methylcholanthrene-induced leukemia in CBA mice.

Thus, it would appear that the rate of growth of lymphoid tissue can be restricted by limiting the intake of protein or essential protein constituents. In this regard, therefore, lymphoid tissue physiology bears a similar relationship to dietary protein as do other cells of the organism, in that nitrogen of a correct quality and quantity must be available.

The importance of diet in the growth of lymphoid tissue has been emphasized further by the apparently high requirement of this tissue for one of the vitamins, pyridoxine. The investigations of Stoerk and his associates[18, 19] have demonstrated a marked involution of lymphoid tissue in rats maintained on a pyridoxine deficient diet. This effect was apparently not due to the diminished food intake or to the mediation of other factors, e.g., endocrine glands. Furthermore, when the pyridoxine content of the diet was very low, the administration of desoxypyridoxine, a pyridoxine antagonist, resulted in a failure of transplanted lymphosarcomas to grow, as well as a regression of established tumor transplants.[20]

Little is known about the possible influence of other dietary components upon the size of lymphoid tissue specifically. Carbohydrates and lipids of the diet can, of course, supply the energy required by the diverse synthetic mechanisms which are concerned with new lymphoid cell construction. It is also clear that in circumstances in which excessive or extra amounts of lipid are processed, there is a generalized sparing of the proteins of the tissues, including those of lymphoid structures.

From the evidence which is available, it may be concluded that the size and the rate of growth of lymphoid tissue are influenced markedly by endocrine and dietary factors, as well as by a variety of physical and chemical stimuli, many of which exert their effects via an endocrine mechanism, namely, the pituitary-adrenal cortical axis. In addition, the response of lymphoid tissue to dietary, endocrine and other factors may be modified by a genetic factor.

In conclusion, let us look briefly at the suggested functions of lymphoid tissue, inasmuch as the quantity of this tissue may bear a relationship to its capacity to fulfill its normal functions. It is well recognized that lymphoid tissue and the lymphocyte have a role in

resistance. The fact that the lymphocyte is one of the end cells on which adrenal cortical hormones exert an influence serves to integrate the roles of the lymphocyte and the adrenal cortex in resistance. In the immunized animal, lymphocytes contain antibody globulin,[21-23] and these immune proteins may be synthesized in lymphoid structures. In addition, lymphocytes may function in the attenuation of viral agents, and the lymph nodes act as filtering beds for the removal of infective and particulate materials. It is probably not an accident that lymphoid cells are found in large numbers at the chief portals of entry into the organism, where the attenuation or removal of, and development of immunity against, invading organisms is of prime importance.

On the basis of these various functions, it seems reasonable to conclude that normal development, growth and proliferation of lymphoid elements serve to make possible the manifestations of the normal functions of these cells. It may also be suggested that acute involution of lymphoid tissue, as a consequence of stress, trauma, or any of the diverse stimuli known to cause lymphoid tissue dissolution either directly or via the pituitary-adrenal cortical mechanism, could release from their imprisonment any infectious or otherwise deleterious agents which may have been trapped in the lymphoid structures. It remains for further experimental work to establish whether this working hypothesis is the basis either for complications of mild infections, which augment pituitary-adrenal cortical secretion, or for the precipitation of symptoms of certain viral diseases following stress. With this concept, it might be possible to account for the practical experience of lymphoid tissue being at the same time both a defense barrier and a source of potential danger.

Some of the data presented in this paper were obtained in investigations aided by a grant from the Division of Research Grants and Fellowships of the National Institute of Health, United States Public Health Service.

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DISCUSSION

ARTHUR W. PROETZ, M.D.: Dr. White has told us of the effects of the adrenal hormone on the lymphoid tissue and mentioned certain other things which have similar effects.

I would like to ask whether the substances closely related to epinephrine, such as ephedrine and similar compounds used freely in our specialty have been known to have any effect on the involution of lymph tissue.

HENRY M. GOODYEAR, M.D.: I not only wish to express my appreciation of this wonderful paper that we have had this morning but I think we also are indebted to Dr. Hill for his keenness and his thought in this matter of bringing Dr. White to us.

I would like to ask Dr. White what influence the use of iodine has upon hypertrophy of lymphoid tissue. In cities where large amounts of chlorine are used in the water, which displaces the iodine, children have a tendency toward an unusual amount of lymphoid tissue and usually the giving of iodine seems to reduce this.

DR. ABRAHAM WHITE (closing): Both questions are very good ones and I regret very much that I don't have the answer to either.

I merely would like to point out that small doses of a variety of substances that we have tried will produce some degree of augmentation of pituitary adrenal-cortical secretion and involution of lymphoid tissue in the normal animal. It happens that ephedrine and iodine are two substances which we have not tried. It would be interesting to conduct these experiments.

RADIUM AND THE LYMPHOID TISSUE OF THE NASOPHARYNX AND PHARYNX

A NEW UNIVERSAL APPLICATOR

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Introduction. In the brief discussion that follows your essayist proposes to limit his remarks to the use of the ionizing radiation of radium in the nasopharynx and pharynx for the reduction of lymphoid tissue causing definite symptoms, the difficulties of the complete surgical removal of which make such radiation not only the most convenient but the most efficient treatment.

Ionizing Radiation. Radium and its emanation, radon gas, have exactly the same characteristics in that they constantly emit three types of radiation: (1) Alpha rays which are positively charged helium nuclei; since these cannot pass through the wall of the Monel metal capsule used in treatment, they require no further consideration; (2) beta rays, comprising about 80% of the radiation, which are negatively charged electrons of varying high speeds up to that of light rays; their chief characteristic is their comparatively mild ability to penetrate living tissue; it is estimated that 93% are absorbed and exert their effects in the first centimeter of tissue; (3) gamma rays, forming about 20% of the radiation, which are composed of electrons having no electric charge, moving with the speed of light and having a very short wave length; they are exceedingly penetrating, some passing through 12 in. of solid lead; when they are stopped in the tissues they scatter electrons which act like the beta rays and thus ionize tissue cells.

For comparison, we may note that the modern x-ray tube emits (1) cathode rays which are essentially the same in physical characteristics and biologic effects as the beta rays of radium, and (2) gamma rays which are exactly similar to those of radium. Thus it is readily understood that the effects of x-rays and the beta and gamma rays of radium and radon in the living tissues are exactly the

same. The rays are absorbed by tissue cells, and the energy thus released ionizes the living cell and causes its gradual death. Tissues vary greatly in their sensitivity to such radiation; it is fortunate that the small round lymphoid cell which is the chief component of adenoid tissue is fairly radio-sensitive, especially when it is newly formed in the germinal centers of lymphoid tissue. It is on this greater sensitivity over that of epithelial and connective tissue cells also present that our radiation therapy is based. The total effect of properly administered radiation is a slow reduction in the size of smaller masses of lymphoid tissue, so that each flattens and becomes much thinner, and any folds, pits or crevices in the tissue are widely opened or completely obliterated.

The Standard Radium Applicator. The present day method of the use of radium in the nasopharynx is by the employment of the Monel metal capsule, which is 25 mm long, with walls of 0.3 mm thickness, and containing 50 mg of pure radium sulfate in its center section of 15 mm. This capsule is brazed to a stiff brass rod and has a small handle. In use it is passed along the floor of the nose until the capsule is in the nasopharynx, in close contact with the mouth of the eustachian tube and the area just posterior to it. The method is essentially beta radiation of comparatively low penetration. The action is directly on adjacent lymphoid tissue without the interposition of any tissue except the overlying epithelium. It is this directness of application and action which constitutes the great advantage of radium over x-radiation of the lymphoid tissue in the nasopharynx and pharynx. Since the x-rays must be applied from outside the head, much normal tissue is exposed to the rays as they pass before the lymphoid tissue is reached, and the overlying skin is most heavily acted upon by the radiation. Radium in the nasopharynx would seem far preferable as more effective, more readily controlled and with no greater danger than external x-radiation.

Radium Dosage in the Nasopharynx. Accurate measurements of the radiation from the Monel metal capsule are not easy to make. Measurements of the surface action by the fogging of photographic film are reasonably accurate, but the dosage in the depths of living tissue can only be estimated mathematically. Schulz and Robbins[1] state that the standard applicator yields about 150 r per minute at the tissue surface. This is reduced to about 47 r per minute at a depth of 2 mm, and to only 10.5 r per minute 5 mm below the sur-

face. This amounts to about 1800 r to the surface tissues in close contact with the center area of the applicator in the usual 12-minute treatment. This dose approximates 800 r 1 mm below the surface. This is greater than the usual dose of x-rays when they are given in the amount of 125 r to each of two skin areas on each side of the head, and repeated in one week, approximating in all about 1000 r. It is thus evident that we are using a fairly heavy dosage to the surface tissues with the radium capsule.

Crowe and others have estimated that the maximum standard dose with the 50-mg applicator is 12 minutes. A very great number of clinical tests with this dosage reveal that it well below the erythema dose in the nasopharynx. Such a dose may be safely repeated after an interval of two weeks, if no clinical reaction follows the first treatment. Three or four such treatments may be given in one series, at the same interval of two weeks. No further dosage should be given for at least six months, and then only after careful determination that there is a real need for further radiation.

The Uses of Radium in the Nasopharynx. Radium irradiation of the lymphoid tissue of the nasopharynx is used for (1) recurrent aero-otitis media; thousands of adults were treated by this method in the armed services in the late war.[2] The results in preventing further attacks were almost uniformly successful, and similar effects have been reported quite widely on a much smaller scale in civilian practice. (2) Recurrent acute catarrhal otitis media in children after adenoidectomy, and in adults with visible lymphoid tissue in the nasopharynx near the eustachian tube; the reduction in the size of the lymphoid tissue lessens the liklihood of further attacks of acute otitis whenever the nasopharynx becomes inflamed. (3) Mild high tone deafness in children who have visible but small amounts of lymphoid tissue in the nasopharynx, about the eustachian tube, after adenoidectomy. Crowe and others[3] have noted quite satisfactory results. (4) In an endeavor to prevent recurrent secondary bacterial infections of the middle ears and paranasal sinuses following virus upper respiratory infection in children with nasopharyngeal lymphoid tissue after adenoidectomy. The radiation reduces the size and thickness of the lymphoid tissue and thus opens the folds, pits or actual crypts in the tissue, in which it seems probable that the bacterial secondary invaders are harbored. Crowe and others[3] have been doing this sort of preventive treatment for more

than 20 years, and their reports in the main are quite favorable. That such radium treatment may also be helpful in some adults with definitely visible, irregular lymphoid tissue, who suffer the same type of recurrent acute bacterial infection of the middle ears or sinuses as complications of virus invasions is a problem that is now being investigated. It will take a considerable period of time before results can be fully measured. (5) In trying to prevent recurrent attacks of acute exacerbation by ascending infection through the eustachian tube from visible lymphoid tissue in the nasopharynx in chronic purulent otitis media with central perforation, by reducing the sourch of the acute infection in the nasopharynx. The same method may be of practical use with marginal perforations with possible cholesteatoma, if operative treatment of these dangerous middle ear infections is refused.

The Use of Radium in the Pharynx. Radium irradiation of the pharynx is proposed for the reduction of the hypertrophy with its consequent chronic infection harbored within the pits and folds of the lateral pharyngeal bands and pharyngeal lymphoid follicles. Such structures often enlarge after tonsillectomy and adenoidectomy in children and are quite common in adults who have had tonsillectomy, or in those who have recurrent acute sore throats, or chronic pharyngeal inflammation centering about these lymphoid bands and patches, when the tonsils are not involved as a cause. Up to the present time, the author has not been aware of any suitable applicator for such treatment; the flexible applicator to be presented will make this type of therapy most easy.

Contraindications to the Use of Radium. Radium should not be used in the nasopharynx for (1) deafness in children when there is a marked high tone loss, and especially when the bone conduction loss as determined by the audiogram is at or greater than 30 db for the same high tones; such children have a true nerve deafness and will almost certainly not be benefitted by radium; (2) nerve deafness in adults; (3) otosclerosis; (4) chronic purulent otitis media without acute exacerbations and in those who have minimal nasopharyngeal lymphoid tissue; (5) with any trace of atrophy of the mucosa of the nasal cavities, the nasopharynx or the pharynx, and (6) in such localized lesions as congenital pits, bursae and crusts in adult nasopharynges; other treatment is essential in such conditions.

Relative contraindications to the use of radium are (1) after

recent acute upper respiratory infection; (2) after recent acute otitis media or acute exacerbation of chronic purulent otitis, (3) in the presence of large masses of lymphoid tissue in the nasopharynx; such tissue must first be reduced as much as possible by appropriate surgical removal. Beta radiation can only produce marked good effects when applied to comparatively thin lymphoid tissue, because of the low penetrating power (4) when there has been recent radium or x-ray application to the head or the nasopharynx for any reason.

The Abuse of Radium Therapy. It should be clear that the determination for the proper use of this powerful agent rests squarely upon an accurate diagnosis of the presence of visible lymphoid tissue in small to moderate amounts only. Such diagnosis calls for the skilful use of the postnasal mirror, or the electric nasopharyngoscope, or both. Anyone without the necessary training, skill and experience to make such an accurate diagnosis should not be using radium in the nasopharynx. When it is used for conditions in the ear, it is further necessary that the exact nature of the aural pathology be first determined, and to interpret the audiogram of any hearing loss; anyone who cannot properly do this should not be using radium.

It would seem proper in the light of this hinging of the use of radium on a careful and accurate diagnosis that radium applicators should only be in the possession of qualified otolaryngologists, and that their issuance to others should not be allowed. Even when the diagnosis has been made by the otolaryngologist, he must most carefully supervise radium treatment given under his direction as by an assistant or nurse.

The indiscriminate use of radium, especially in adults, or as a mere routine after adenoidectomy in children is to be condemned. It is being used by some without an accurate diagnosis for such vague purposes as to "prevent colds," to "cure" what Proetz has called the great American nightmare, postnasal drip, and for tinnitus and deafness which are clearly due to internal ear disturbances or to otosclerosis, and even as a routine treatment whenever there is a little patch or two of atrophic lymphoid tissue somewhere in the nasopharynx. Radium is a powerful agent to be most carefully used, since its potential dangers are not yet fully known.

The Dangers in the Use of Radium. The dangers in the use of radium in the Monel metal applicator are those involving the *operator* such as (1) an acute overdose with burning of the skin by the incomprehensible accident of carrying the bare applicator in the pocket; (2) insidious damage to the fingers by repeated small doses, which can lead to atrophy of the skin and nails and possibly much later to ulceration and epithelioma. The applicator is said by Schulz and Robbin[1] to have an ionizing radiation of 10 r per hour at the end of the handle, while half way down this dose is quadrupled. The applicator when out of its lead safe must always be handled with dispatch, and the capsule never touched with the fingers. A long-handled brush must be used to cleanse the applicator after use. If many treatments are being given the use of lead rubber x-ray gloves is advisable. (3) Damage to the hematopoetic system with anemia and leukopenia by long continued, very small exposure to the gamma radiation. Schulz and Robbins[1] state that a total body radiation of only 0.1 r per day is now considered to be the tolerance level for the blood forming organs. The 50-mg applicator repuires 2 cm of lead to reduce the gamma radiation to this level at a distance of one meter, and 7 cm of lead at one-half meter. The applicator must always be stored in its carefully closed lead safe 20 ft. or more from anyone such as secretary, nurse or doctor who may be exposed through the usual eight-hour day. The operator should retire from the treatment room during the time the applicator is in the nasopharynx, although sore means of quick recall must be provided when necessary. The mother or other relative should stand by the child during treatment for reassurance and control, rather than the operator. (4) Since the gonads are highly sensitive to ionizing radiation it is usually advisable when many treatments are being given for the operator to wear the lead rubber apron as used in fluoroscopy. At all times it must be remembered that distance is the best protection against damage due to repeated though small exposures.

Dangers to the *patient* are (1) an acute overdose with local erythema, edema or blistering; this must always be prevented by the most careful timing of each dose and by close control of the patient during the treatment; (2) late effects such as atrophy of the mucosa, telangiectasis, ulceration and perhaps even malignant new growth. These should never occur if doses well below possible erythema levels are always given, and the method not abused by giving more than three or four treatments in any one series, care-

fully spaced, and not more than one such series in six to twelve months.

A New Universal Nasopharyngeal and Pharyngeal Radium Applicator. The author wishes to present a new type of flexible radium applicator. It is of the same general measurements as the standard rigid applicator, except that the cannula has a little greater diameter (Fig. 1); it will nevertheless slip through all but very badly obstructed nasal chambers. It consists of a rigid, straight cannula having a conical handle with an indicating ring. The terminal 7.5 cm of the operative end is made of a flat, flexible spiral spring into the free end of which the standard 2.5 mm Monel metal radium capsule is firmly fixed. A heavy straight wire stylet is provided.

When the wire stylet is in place within the cannula, the applicator is straight and rigid and can be used in the way in which the present standard applicator is employed (Fig. 2A). This will adequately reach lymphoid tissue in and immediately about the eustachian tube orifice and the area just posterior to it. When there is lymphod tissue above and behind the tube (Fig. 2B) or below and behind the tube orifice (Fig. 2C), the withdrawal of a part of the wire stylet allows the natural curve of the spiral spring of the universal applicator to bring the radium capsule into really close contact with such areas. Since we have seen that close contact is required for the full ionizing effect of any calculated dose of radiation, the flexible applicator offers advantages that are impossible with the rigid applicator. The manufacturers of the standard applicator strongly advise against bending the brass rod in endeavors to more nearly reach areas other than the eustachian tube mouth, for fear that the radium capsule may be opened by so doing and the radium scattered. The flexible applicator enables one to reach any lymphoid tissue in the nasopharynx without making such precaution necesary.

A further very great advantage of the flexible applicator is that it allows for the first time accurate and comfortable radiation of the lateral pharyngeal bands and pharyngeal follicles. Under mild local anesthesia of the floor of the nose and the side of the pharynx, the applicator with its stylet in situ is passed into the nasopharynx through the nose, with the indicating ring turned down (Fig. 2D). Withdrawal of the stylet completely out of the flexible

portion allows it to turn through a right angle, so that it lies with the radium capsule in close contact with the lateral band throughout most of its length.

At present an initial dose of six minutes is given on each side. Later doses of eight minutes are used at intervals of two weeks, if there has been no visible reaction or soreness after the first radiation. From three to five such treatments are given; the number of sessions will depend on the thickness and width of the lateral bands, and on the effect of previous treatments.

The method offers gradual reduction in size of these structures by a technique that is very easy and comfortable for the patient. The action is so very much more direct and controllable than by external x-radiation that it seems greatly preferable. While the lateral bands and pharyngeal follicles should always be punched or dissected off during adenoidectomy in children, this operation has never been widely accepted for adults. This is probably because of the demand made on the co-operation of the patient if the operation is done under local anesthesia, and a natural reluctance to use general anesthesia for such a comparatively minor procedure. The pharyngeal bands and patches can also be removed by piecemeal electrocoagulation, but time has shown that the process is slow, recurrently painful and often marked by repeated secondary bleeding.

CONCLUSIONS

1. A brief summary of the rationale, the technique, the uses and contraindications, the abuse and dangers of the employment of the standard Monel metal radium applicator in the pharynx is presented.

2. A new type of flexible applicator is presented by which practically any area of the nasopharynx can be easily reached for accurate dosage, and which can also be used to apply radiation to the lateral pharyngeal lymphoid bands and patches with accuracy and ease.

Note: The metal cannula for the universal applicator is made by G. S. Pilling and sons, of Philadelphia. The radium capsule is supplied and attached by the Radium Chemical Company. The author especilly desires to thank Mr. George Loftus of the Radium Chemical Company for his invaluable help in developing the new applicator.

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DISCUSSION

JOHN G. MCLAURIN, M.D.: I wish to describe an experience with a radium applicator that I formerly devised but would now consider obsolete.

For many years, I have been very much interested in headaches of otorhinological origin and, of course, this meant that I would frequently encounter headaches that were typically those referred from ethmoid and sphenoid diseases. In such headaches of intractable type where sufficient pathology appeared in the ethmo-sphenoidal area to justify surgery, I frequently did an exenteration of the ethmoids and removed a sufficient amount of the front wall of the sphenoid sinus to assure good ventilation and drainage. In some instances, however, the headache that was referred from sphenoidal blockage would recur and I almost invariably found that this resulted from a closure of the sphenoid sinus.

I believe that we have all been taught that in removing the front wall of the sphenoid, it was considered better technic to avoid the punching away of the thick or cancellous bony structure. I came to the conclusion that this regeneration of the wall was frequently the result of an osteogenetic process that followed the punching out of cancellous bone tissue. The recurring headache that took place when the bony wall closed to the point of interfering with ventilation could be relieved invariably by again punching out the wall and regaining good ventilation to the sphenoid sinus.

After having this trouble with several cases I decided to take some of the material that I subsequently punched out from the front wall for biopsy and in some instances I found that I was dealing with an osteogenetic process; in other instances the microscopic study of the tissue showed that I had a true lymphoid gland hypertrophy that was responsible for closing the opening that I had made. When the opening closed, the pain was usually referred to the occipital area and sometimes to the frontal area just above the inner canthus and occasionally to the canine fossa.

After opening several of these sinuses on numerous occasions and having them close promptly, I decided that something more had to be done to make them stay open. I tried various strengths of silver nitrate, applied to the edges to try to avoid a closure and encourage the healing of membrane across the edge. I then decided to use radium at the edges of the opening. You may recall that in about 1939 to 1941, the radiologists were using a radium needle that contained 9.6 mg of radium. They buried these needles in tissue surrounding malignant processes and would leave them for a considerable length of time, usually for several days. Since there was no radium nasal applicator on the market at that time, I devised an instrument that was made in the following way. I took a No. 2 Eustachian cannula and spread the lumen at the tip for about 2 or 3 mm

back so that one of these radium needles would fit into the tip. Of course, the needle had an eye in the base of it and through the eyelet I tied a very fine wire which I brought back through the cannula and tied around the loop at the handle of the cannula. I would then place the needle so that the radium chamber of it straddled the edge of the sphenoidal opening and left it in site for twenty to twenty-five minutes at intervals of one week. As a rule, after three or four such aplpications there was a perfectly smooth healing across the opening and the sphenoidal opening had no tendency to reclose. As a result of this, the sphenoidal headache was relieved.

Since Dr. S. J. Crowe reported the use of his monel metal applcator, I have been using that type of applicator to accomplish the same thing but I have left it in site for from eight to ten minutes and found that an average of three doses at intervals of one week to ten days insured a healing so that the sphenoidal opening persisted. At the time that I was doing this work with the instrument that may now be considered obsolete, I noticed a definite atrophy of lymphoid tissue in the immediate area of the pharynx but I did not report this and the procedure was not being done for the same reason that Dr. Crowe was using radium. In other words, the primary purpose of Dr. Crowe's work has been to produce as nearly as possible a disappearance of lymphoid tissue in the orifice and inner portion of the Eustachian tube to insure a patency of the tube. Please understand that I am not trying to take away from Dr. Crowe any of the glory that is due him as a result of his valuable reports on this work. I did, however, notice that there was an improvement in the patency of the Eustachian tube and was rather inclined to believe that the improvement had resulted from the clearing up of an ethmo-sphenoidal infection that drained over the orifice of the tube, rather than an atrophy of the lymphoid tissue in the Eustachian orifice.

In closing, I wish to sound a warning regarding the use of radium in the pharynx. I am quite sure that we should be very accurate regarding our observations before radium is used. In other words, we should be reasonably sure that lymphoid tissue overgrowth does exist and is probably responsible for a closure of the orifice or inner third of the tube. This can be determined as a rule by careful nasopharyngeal examination with a nasopharyngoscope. The warning that I am giving is the result of the fact that I believe that in some instances we may have an uncomfortable pharynx because of a diminished output of mucus from the glands in that area. I am inclined to think that there may be a relatively dry pharynx in some instances. Of course, one should also consider what the effect of radium may be when applied in such proximity to the pituitary gland. So far, I have not seen any ill effect but the procedure is relatively new and I think the indications for the use of radium should be quite definite.

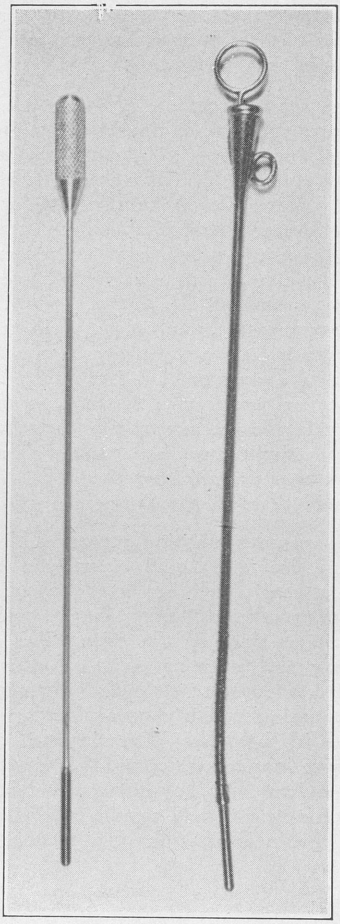

Fig. 1.

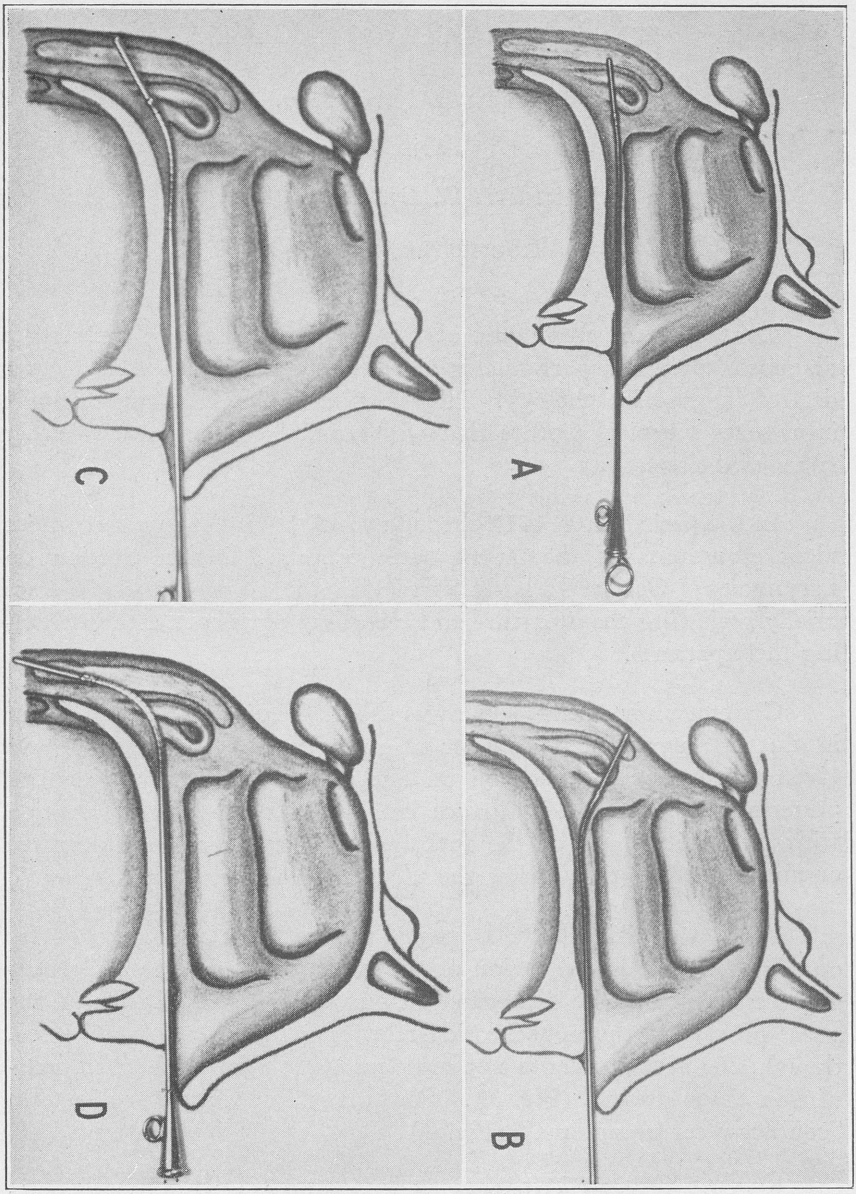

Fig. 2.

CONTACT ULCER GRANULOMA

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AND

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Contact ulcer granuloma of the larynx presents an interesting diagnostic problem, particularly to those who have not seen a great deal of laryngeal pathology. However, to the trained laryngologist it presents a typical picture that will rarely be confused with other types of diseases.

In the period from 1937 through 1946, 53 patients with contact ulcer granuloma of the larynx were examined in the Section on Laryngology, Oral and Plastic Surgery of the Mayo Clinic. We are briefly reviewing the literature and recording our experience in treating these patients.

Contact ulcer of the larynx was first defined in 1928 by Jackson[1] in this manner: "Contact ulcer of the larynx is the name I have given to superficial ulceration on one or both sides of the larynx posteriorly, the ulcerated surface coming in contact on phonation with that of its fellow on the opposite side, the latter being ulcerated or not, according to whether the ulcer is monolateral or bilateral."

When viewed with the laryngeal mirror the ulcer is seen partly on edge (Fig. 1) in the region of the vocal process. One may actually see a tiny cuplike depression on one side (Fig. 2) in which the vocal process of the opposite side rests on phonation. More often, though, the actual ulcer is not seen because of the exuberant granulation tissue present (Fig. 3). For this reason we prefer the term "contact ulcer granuloma" (Fig. 4).

Pathology. The pathology of the condition is one of chronic nonspecific inflammation. One may find polypoid masses composed of new granulation tissue richly supplied with blood vessels and covered with inflammatory exudate (Fig. 5). On the other hand there

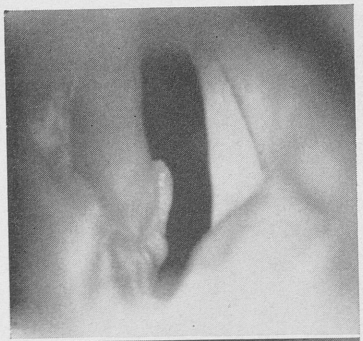


Fig. 1.—Unilateral contact ulcer granuloma. Only the edge of the granuloma is visible.

Fig. 2.—Bilateral contact ulcer granulomas. Note the cupping of the granulomas.

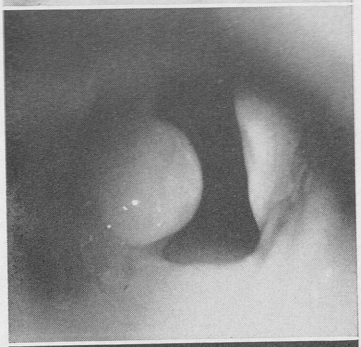


Fig. 3.—Unilateral contact ulcer granuloma. Note the mammillated appearance.

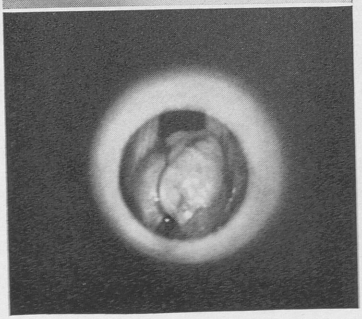
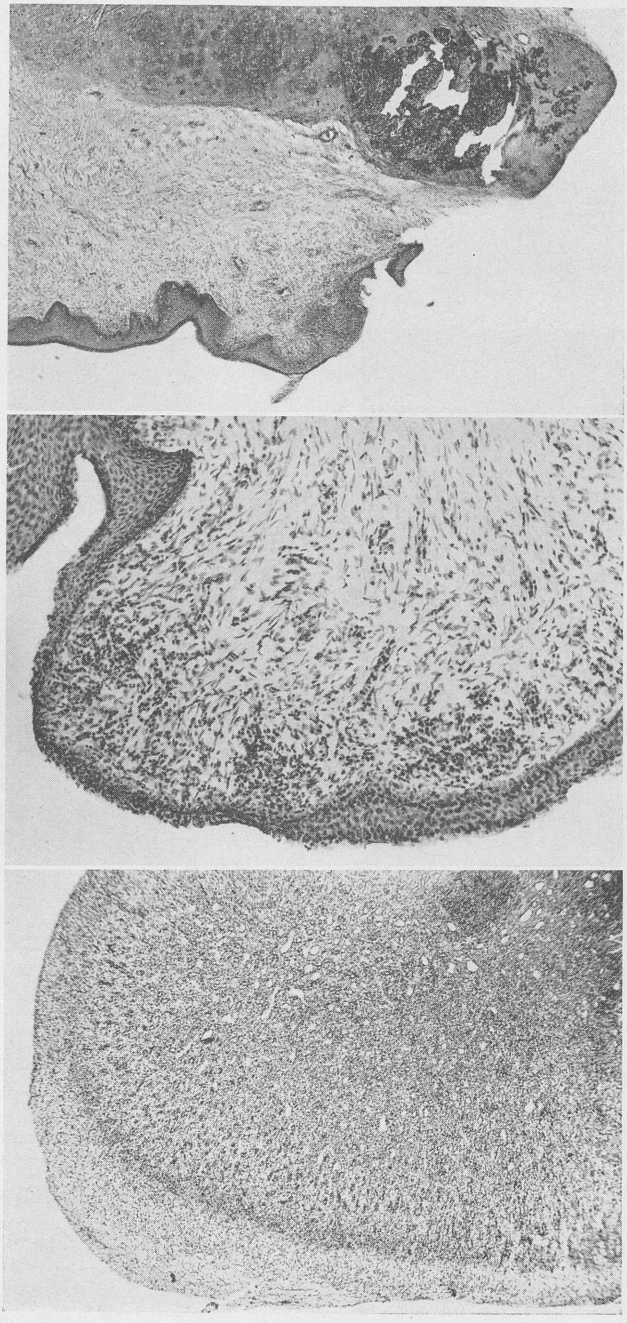


Fig. 4.—Bilateral contact ulcer granulomas with vocal cords attempting to approximate.



may be small, hard, fibrous nodules composed of inflammatory fibrous tissue with few blood vessels, the whole covered with epithelium (Fig. 6). The cartilage of the vocal process may be surrounded by the granulation tissue (Fig. 7) or found in the floor of the ulcer. Loose cartilage may be free in the granuloma.

Symptoms and Etiology. The patient complains of discomfort in the larynx, hoarseness which may be slight, or pain extending to the ear, and sometimes hemoptysis and chronic cough.

Vocal abuse is the chief etiologic factor in the production of a contact ulcer granuloma. The mechanical hammering of one vocal process against another apparently causes ulceration of the mucous membrane over the vocal process. In those instances in which contact ulcer granuloma follows tracheal intubation the chief etiologic factor is also a mechanical one. In all probability the intratracheal tube produces an ulcer in the larynx either by pressure necrosis or by trauma.

Tracheal intubation for general anesthesia was introduced by Elsberg[2] in 1910. For many years, few physicians, if any, were aware that this procedure could in some instances be followed by contact ulcer granuloma. Clausen[3] in 1932 was the first to report a case of contact ulcer granuloma following intubation. We have been able to find eight additional cases[4-10] in the English and American literature (up to March, 1947) which, with the nine cases of our own, makes a total of 18 cases.

Fig. 5.—Contact ulcer granuloma. Note the blood vessels and exudate.

Fig. 6.—Epithelized contact ulcer granuloma with fibrosis.

Fig. 7.—Contact ulcer granuloma. Note the necrotic cartilage.

Treatment. Most writers in general have recommended a plan of treatment which consists of surgical excision of the granuloma and removal of part of the vocal process if it is exposed, prohibition of irritant medication or swabbing, and absolute silence. Most authors agree that ultimate recovery takes place as a rule, but progress has been slow in most instances and repeated excisions are often necessary.

Some[11] have expressed the belief that cauterization of the bed of the ulcer is bad because of the superficial character of the lesion and the proximity of the crico-arytenoid joint. On the other hand, in 1938 Howard[12] used fulguration for contact ulcer granuloma with excellent results. In his opinion fulguration definitely hastened recovery. Surgical diathermy has been used for practically all of the patients treated at the clinic for the last ten years and no ill effects have been noted.

In our practice the hypopharynx and larynx are cocainized with 10% solution of cocaine and the patient is anesthetized with intravenously administered thiopental sodium (pentothal sodium), supplemented by curare (d-tubocurarine chloride). Suspension laryngoscopy is used to expose the larynx. The granuloma is removed with cup forceps and the base of the wound is touched with surgical diathermy.

After a few days the patient is sent home on a regimen of absolute silence with instructions to return in one month for examination. At the end of the month if the granuloma has not recurred or is definitely smaller we continue with observation at periodic intervals. On the other hand it may be necessary to repeat the removal of the granuloma.

It is important to wait at least one month or longer between operations. In this way the ulcer gets a chance to heal without being stimulated by repeated intervention.

We noticed that if the throat symptoms had been present for months or years rather than weeks, there was more chance of getting the patient well with only one operation. There are exceptions to this, particularly if the granuloma has been stimulated by silver ni-

trate or recent biopsy. Then, too, it is difficult to determine from the history how long the granuloma has been present.

Often at the time of removal of the contact ulcer granuloma one can judge fairly accurately whether or not there will be recurrence. If the granuloma bleeds readily when touched or is soft and friable when grasped with the cup forceps, there is less chance of getting the patient well with only one operation than if the granuloma is hard and fibrosed.

Woodruff[13] in 1936 explained the high incidence of this disease in men on the basis of the fact that the raspy or throaty method of voice production is seldom used by women. Peacher and Holinger[14] carried this observation to its logical conclusion and cured some contact ulcer granulomas by vocal re-education of the patients with apparently better results than they were able to obtain by surgical excision of the ulcer and absolute silence.

Excision of the contact ulcer granuloma followed by surgical diathermy in conjunction with vocal re-education seems to us to be the ideal method of treatment. Excision affords a means of obtaining a biopsy specimen. In this way the clinical impression of contact ulcer granuloma can be verified by microscopic examination of tissue removed. In three instances during the period from 1937 through 1946, microscopic examination of tissue removed from the larynx showed the clinical impression of contact ulcer granuloma to be wrong. In one case the pathologic diagnosis was myxomatous tissue, in another it was squamous cell epithelioma, grade 2 (Broders' method), and in a third the diagnosis was hemangio-endothelioma imitating hypernephroma.

TABLE 1

CONTACT ULCER GRANULOMA

Indeterminate etiology	44
After intratracheal anesthesia	9
Total	53

Analysis of Data. Fifty-three patients with contact ulcer granuloma were examined in the period from 1937 through 1946. We

have divided these cases into two groups depending on whether or not there was any previous history of tracheal intubation. In 44 patients we could find no history of previous tracheal intubation. A much smaller group of 9 patients gave a history of tracheal intubation prior to the onset of their symptoms (Table 1).

Symptoms are similar in the two groups and the gross and microscopic appearances are identical. There are some striking differences however. The contact ulcer granuloma which follows tracheal intubation occurs more often in women than in men (Table 2). We found the ratio of women to men to be 2:1 in our series. In the cases reported in the literature up to March, 1947, the ratio of women to men was 3.5:1. This is in marked contrast with the group in which there has been no history of tracheal intubation. In the latter group the ratio of women to men reported in the literature is about 1:99. We found that all of our patients in this group were men.

TABLE 2

CONTACT ULCER GRANULOMA

SEX INCIDENCE

	M	F
Indeterminate etiology	44	0
After intratracheal anesthesia	3	6
Total	47	6

The contact ulcer granuloma which follows tracheal intubation is more frequent in women than in men, probably because women have a smaller larynx than men. It is doubtful whether length or kind of operation, the route or difficulty of introduction of the tube have anything to do with it. By analyzing our cases and those reported we found that the tube had been introduced through the nose in 10 cases and through the mouth in 8 cases. We found 5 cases in which the lesion followed difficult introduction and 7 cases in which there was no difficulty; in 6 cases this information could not be obtained. The average length of the operation was 127 minutes. The shortest was 37 minutes and the longest was 300 minutes.

The contact ulcer granuloma which follows tracheal intubation is more often bilateral than unilateral, occurring in 7 of our 9 cases (Table 3). The frequency of occurrence of bilateral granulomas in those patients not having had tracheal intubation was only 5 of a total of 44.

Kearney[8] in 1946 said that the benefits of intratracheal anesthesia greatly outweigh its few undersirable sequelae. We agree, and intend to continue using intratracheal anesthesia, realizing that even in the hands of the expert anesthesiologist tracheal intubation can be followed by contact ulcer granuloma. Surgeons should be aware of this fact and if any of their patients, particularly women, complain of hoarseness, pain in the larynx, loss of voice or a choky feeling after tracheal intubation they should see to it that the larynx is examined. Contact ulcer granuloma as a sequela of intratracheal anesthesia is probably not as rare as the few reported cases would lead one to believe.

TABLE 3

CONTACT ULCER GRANULOMA

LOCATION

	Bilateral	Unilateral
Indeterminate etiology	5	39
After intratracheal anesthesia	7	2
Total	12	41

In the group of 44 patients who had no history of tracheal intubation there were 7 who did not receive surgical treatment at the clinic. These patients did not receive treatment for reasons of poor general health, advanced age, small size of the lesion or refusal to have treatment. We were able to follow by letter and personal examination by the patient's physician or at the clinic 30 of the 37 patients treated in this group. In 23 of these the condition was cured with treatment (Table 4).

TABLE 4

CONTACT ULCER GRANULOMA

TREATMENT

	Treated	Traced	Well
Indeterminate etiology	37	30	23
After intratracheal anesthesia	9	9	9
Total	46	39	32

It is of some interest to know how many operations were necessary to get these 23 patients well (Table 5). We found that 8 patients had only one operation, 11 had two operations, 3 had three, and 1 required five operations.

TABLE 5

CONTACT ULCER GRANULOMA

INDETERMINATE ETIOLOGY

NUMBER OF OPERATIONS

PATIENTS WELL

8 patients	had	1 operation each
11 patients	had	2 operations each
3 patients	had	3 operations each
1 patient	had	5 operations
23 patients	had	44 operations

All 9 patients with a history of tracheal intubation received surgical treatment at the clinic for the contact ulcer granuloma. All were cured with treatment. We found that 4 patients were cured with one operation, 4 with two operations, and 1 with three (Table 6).

TABLE 6

CONTACT ULCER GRANULOMA

AFTER INTRATRACHEAL ANESTHESIA

NUMBER OF OPERATIONS

PATIENTS WELL

4 patients	had	1 operation each
4 patients	had	2 operations each
1 patient	had	3 operations
9 patients	had	15 operations

Of the 30 patients with no history of intubation whom we were able to follow, 7 were not cured by the treatment received at the clinic for their contact ulcer granuloma (Table 7). Four had only one operation and of these 3 did not return; one was a physician in active practice. A second operation was not recommended. Of the 3 remaining, 1 patient had two operations, another had three, and 1 had five operations without relief. The last 2 patients were ministers.

TABLE 7

CONTACT ULCER GRANULOMA

INDETERMINATE ETIOLOGY

NUMBER OF OPERATIONS

PATIENTS NOT WELL

4 patients	had	1 operation each
1 patient	had	2 operations
1 patient	had	3 operations
1 patient	had	5 operations
7 patients	had	14 operations

Physicians, farmers, managers, ministers, agents, and salesmen are those who are most likely to get a contact ulcer granuloma (Table

G.F.TUCKER

8). It seems to us too that these patients are of the "nervous" type or live on a plane of high nervous tension. The trip to the seashore that used to be recommended for contact ulcer granuloma may have been beneficial not so much because of the sea air which the patients breathed but because of the rest and relaxation which they found there.

TABLE 8

CONTACT ULCER GRANULOMA

INDETERMINATE ETIOLOGY

OCCUPATION

Occupation	Patients	Occupation	Patients
Physicians	6	Singer	1
Farmers	5	Plumber	1
Managers	5	Carpenter	1
Ministers	4	Laborer	1
Agents	3	Merchant	1
Salesmen	2	Bank clerk	1
Office workers	2	Credit man	1
Miner	1	Miscellaneous	9
Total			44

SUMMARY

With the method we have employed in the treatment of contact ulcer granulomas we have been able to cure 32 of the 39 traced patients. In 23 of these 32 cases the lesion was of indeterminate etiology and in 9 the patients had undergone intratracheal anesthesia. Since the report of Peacher and Holinger[14] we are adding voice education to the treatment, hoping to get still better results.

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LETHAL GRANULOMATOUS ULCERATION INVOLVING THE MIDLINE FACIAL TISSUES

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From time to time there has been presented before this society a group of granulomas having their primary site in the tissues of the nasal chambers or palate, usually running an indolent course for a year or two, sometimes even appearing to heal for a short time but again breaking down for no obvious cause. After a few months to a few years the lesion becomes more active and invades the neighboring bony structures, destroying the nose, palate and maxillary air sinuses, frequently with preservation of the upper lip, resulting in a shocking facial deformity. These patients die either from pure exhaustion or from hemorrhage.

The striking thing about these granulomas is the indolent but inveterate development of the lesions; where from their appearance we expect signs of active suppuration, none is present; the slow destructive advance suggests some sort of malignant lesion or blood dyscrasia. Histologic studies of the tissues of the lesion, of the blood and of the bone marrow have, however, failed to furnish any evidence to confirm this suspicion.

The pathologist studying sections of the diseased tissues appears to be struck by the absence of the usual signs of resistance to infection. Organisms which are found casually invading the tissues without the customary leukocytic barrier being set up do not appear to be the cause of the lesion. With the antibiotics of the present day such an organism may be completely eliminated from the tissues without affecting the progress of the disease. After stoppage of antibiotic treatment another different organism will appear invading the tissues in the same manner.

The bacteriologist and the mycologist have been unable to discover an etiologic agent. As their knowledge of possible causative organisms has increased and their technical skills at isolating possible invaders have improved and multiplied, they have carried efforts at isolating an etiologic factor to great lengths. Recently these efforts

have included implanting material in the allantoid membrane of chick embryos but they have not revealed a causative micro-organism. For this reason the lesion has been termed "idiopathic" by some authors.

A typical pathologic description is that given by Hoover.[1] He stated: "On the border of the lesion is an amorphous mass of necrosis, beneath which there is an infiltration by inflammatory cells, chiefly lymphocytes and macrophages, with occasional plasma cells. A few polymorphonuclear leukocytes are also present. There is some new formation of capillaries. The larger vessels in the tissue show a definite perivascular cuff of lymphocytes and macrophages with degeneration of the arterial walls in some regions. While there are focal accumulations of the infiltrating cells in the tissues the lesion is not characteristic of tuberculosis, syphilis or leprosy. The diagnosis is that of a chronic granuloma of unknown cause." The pathologist added that the lesion suggested the Arthus phenomenon.

This lesion has received different names from different authors, being termed "granulomatous ulcer of the nose and face" by Hoover,[1] and "osteomyelitis necroticans faciei" by Rasmussen,[2] who concluded, after reviewing the literature and studying two cases of his own, that "the morbid process is assumed to be a disease sui generis." Lewy[3] termed the condition, "gangrenous osteomyelitis of the paranasal sinuses;" Lierle,[4] "chronic infectious ulcer of the nose;" Arrowsmith[5] and Myerson,[6] "gangosa" and Isbell,[7] "chronic granulomatous ulcer of the nose of unknown cause."

The most vivid and accurate clinical description is that given by Stewart.[8] If the term "midline of the face" is substituted for "nose" his title, "lethal granulomatous ulceration of the nose," seems most descriptive of the condition, and I feel should be accepted generally.

Stewart[8] stated: "During the past ten years several cases of a peculiar type of ulceration of the nose, which correspond to no known pathologic entity, have come under our direct observation. The ulceration was progressive and invariably ended fatally."

Stewart[8] divided the symptomatology of the disease into three stages, the first or prodromal stage, the second stage or period of active disease and the third or terminal stage.

The prodromal stage, Stewart[8] pointed out, may last from a month or two to as long as four or five years. At first the patient may merely be conscious of a stuffiness in the nose, sometimes accompanied by a watery or serosanguineous discharge. On the other hand the initial expression of the disease may be a superficial ulcer in the roof of the mouth or in the gingivobuccal groove. Some patients appear to have had infection in the paranasal sinuses preceding the onset of the first symptoms of lethal granuloma; in others a history or findings suggesting a preceding chronic infection of these structures cannot be obtained. A superficial ulceration of the septal mucosa, thought to be on a traumatic basis, may appear and disappear. If a submucous resection is done, a perforation usually will result.

The second stage, Stewart[8] termed the period of active disease. The patient's nasal obstruction may be associated with a small brownish ulcer on the septum, inferior concha or roof of the mouth, covered with a gelatinous crust which on removal shows a shallow ulcerating surface. The discharge is purulent or sanguinopurulent and has a foul smell. The disease tends to spread from the palate to the inside of the nose and from the inside of the nose to the outside, so that early in the active stage the tip of the nose may become swollen and indurated. The disease progresses and sequestra of the nasal bones, the malar bones and the palatal bones may come away. Abscess formation may take place under the cheek and may require drainage. There may be a little fever with an irregular temperature and very moderate leukocytosis or even leukopenia. The polymorphonuclear leukocytes tend to maintain their normal proportions in the blood picture. Agranulocytosis has never been found and septicemia, as indicated by blood cultures, is absent. Except for a rather pronounced weakness and lassitude the patient may present a curious impression of well-being in spite of the serious appearance of the advancing lesion.

In the third or terminal stage Stewart[8] stated that the obvious exhaustion of the patient is an outstanding clinical feature. The facial appearance is monstrous. The eyelids are swollen and purulent discharge trickles from between the lids. Sloughing areas appear over the lacrimal sacs and cheeks and the soft tissues about the external nose disappear, perhaps including the upper lip. The mutilating destruction may be extreme. The hard and soft palates may

be completely destroyed. Through the large central aperture in the face, the tongue, the roof of the nose and the nasopharynx may be plainly visible, together with the roofs of the maxillary air sinuses exposed by ulcerative destruction of the lateral walls of the nose. The posterior pharyngeal wall may be covered with dirty gray necrotic material. The tongue remains unaffected and sequestration of the basisphenoid has never been observed. The patient may die of hemorrhage from erosion of large vessels, which are troublesome to control in a necrotic region the bony walls of which have been destroyed. However, usually he appears to die from simple exhaustion.

Stewart[8] summarized his clinical description by stating that the picture is one of progressive destruction of the nose, face and pharynx. The duration of the illness is from a few months to as long as five years. The most striking feature of the disease is the apparently complete absence of resistance on the part of the patient to the progress of the disease.

This vivid description of a baffling disorder can hardly be improved on.

In Hoover's extensive review[1] of the literature he was able to find approximately 60 cases of lethal granulomatous ulceration of the facial tissue including his own case. Rasmussen[2] in a later review was able to find only 33 cases which he felt were similar to his own. It is of course difficult to tell how many of the earlier cases might reveal a causative micro-organism if studied at the present time. Even now when we consider how few viruses may be present in a granuloma which they are causing, it is impossible to rule out absolutely the presence of this type of organism. Until such time as we can show definitely that such an organism is the etiologic factor, however, we must consider "lethal granulomatous ulceration of the midfacial tissues" an idiopathic disorder. As the name implies, this disorder has proved refractory to all treatments tried, although they have been many, varying from the use of iodides and mercury through roentgen therapy to the antibiotics.

From the purely clinical standpoint it seems apparent that there is nothing in the gross appearance of these "idiopathic" lesions to differentiate them from specific infectious granulomatous ulcerations occurring in the same locations. Clinicians experienced in ob-

serving gangosa feel certain that the case under consideration is an instance of this disorder. Indeed, except for the prognosis and the geographic area from which the patient comes, there is nothing to differentiate the two conditions. The controversy as to whether gangosa is an instance of tertiary syphilis, occurring in a particular race, need not be entered into here.[9-11] Yet clinicians experienced in observing the destructive lesions of tertiary syphilis about the face are certain the condition is syphilis and are amazed by the lack of confirmatory laboratory findings. The same thing holds true for those specializing in tuberculosis. They feel certain the lesion *must* be tuberculous. Another will insist on blastomycosis or leprosy or oidiomycosis. Pathologists are careful to report sections taken from these lethal granulomas as being not "typical" or "diagnostic" of this or that condition, being prepared to admit that an atypical example of any one of the specific granulomas might be present.

In considering the reported cases and studying those encountered at the Mayo Clinic several pertinent questions arise. Is there a reason why the gross clinical pictures in the granulomas of unknown origin and in those of known origin are indistinguishable and why the histologic pictures in granulomas of whatever type have a basic identity with a by no means invariable modification produced by the etiologic agent? Why does the preferred site of the lesion appear to be the midline tissues of the face? Is there a reasonable hypothesis to explain the rare occurrence of these facial granulomas without an etiologic agent being demonstrable? What is the physiologic mechanism by which such a lesion can be produced? Why do patients with "idiopathic" granulomas show an almost complete lack of that physiologic activity known as resistance? Is there a single mechanism by which all these seemingly diverse phenomena could be produced? What therapeutic implications can be drawn from consideration of any possible causative factors that may be hypothesized?

Baker,[12] in discussing tissue changes in fungous diseases, found that, when they were tabulated in respect to the degree of suppuration, macrophage and giant-cell response, caseous necrosis and fibrosis, several of the deep fungous infections such as blastomycosis (North and South American), coccidioidomycosis, sporotrichosis and moniliasis showed all of these tissue changes. Others of the deep infections such as actinomycosis, nocardiosis and maduromycosis, showed

all these changes except caseous necrosis. He felt that tissue changes in fungous infections represent response to proliferating and dying foreign bodies and in some instances may represent a hypersensitivity to the presence of an endotoxin. It would seem evident from this report of Baker that in fungous infections at least the body is reacting in a stereotyped manner to the whole group of fungi although some relatively unimportant modifications are produced by the specific organism. To put it in another way, resistance to such organisms uses the same immunologic mechanism in each instance.

It might be enlightening to list under the causative organism involved the various ulcerating lesions of the facial tissues from which it has been suggested that lethal granulomatous ulceration must be differentiated. They are: 1. *Bacillaceae*: *A.* Anthrax. Jordan and Burrows[13] pointed out that Bacillus anthracis is the only member of that large group pathogenic for man; 2. *Parvobacteriaceae*: *A.* Glanders; 3. *Mycobacteriaceae*: *A.* Tuberculosis; *B.* Leprosy; 4. *Fungi*: *A.* European blastomycosis (torulosis); *B.* American blastomycosis (oidiomycosis); *C.* Coccidioidomycosis (valley fever); *D.* Rhinosporidiosis; 5. *Treponemataceae*: *A.* Syphilis; *B.* Yaws, and 6. *Protozoa*: *A.* Leishmaniasis.

It is immediately apparent that diseases caused by the Eubacteriales, the organisms most commonly thought of in the infections which we meet in the human, are not included in this list. Even with the Eubacteriales it is only in response to those members of the group actively producing toxin that suppurative inflammation results.[14] Bacterins or bacterial proteins produce antibodies of a feeble reactivity in so far as humoral antibodies are concerned.[15] The character which all the organisms enumerated hold in common is the fact that they are slow or meager producers of exotoxin (or simply toxin).

In responding to the environmental stress produced by invasion by micro-organisms, Forbus[14] stated, the body makes use of two stereotyped defense mechanisms, suppurative and granulomatous inflammation. In the first the responding cell is the polymorphonuclear leukocyte; in the second, the cells of the reticulo-endothelial system, especially the macrophage. He found that both suppurative and granulomatous inflammation may be either acute or chronic. A

third type of inflammation, which he characterized as being a mixture of the other two, also exists.

The cells of the reticulo-endothelial system in granulomatous inflammation undergo many successive morphologic changes. These are proliferation, degeneration, death and dissolution, phagocytosis, mobilization and antibody production. In terms of the biologic properties of the reticulo-endothelial cells the proliferative reaction is at times so enormous that the lesions often appear to the clinician and even to the pathologist as tumors. This is responsible for the term "granuloma," introduced when the distinctions between hyperplasia and neoplasia could not be so sharply drawn as they are today. The proliferative features of granulomatous inflammatory disease are often so prominent that the clinical observer is overimpressed by these purely secondary features of the disease. These cells that become so abundant must eventually disappear unless the inflammatory reaction is ineffective and the patient dies. Thus necrosis of the reacting cells is *characteristic* of granulomatous inflammation. Two types of necrosis occur: coagulation necrosis as may be seen in the healed and healing stages of Hodgkin's disease, and liquefaction necrosis which is present in those granulomas having the same clinical appearance as the idiopathic type. Characteristic of the granulomas is the fact that differential blood counts have a very limited usefulness indeed in the diagnosis of granulomatous inflammation. In spite of the fact that the reacting cells in granulomas multiply continuously, paradoxically, leukopenia rather than the expected leukocytosis is common. The relative mononucleosis which occasionally may be found constitutes an unfavorable rather than a favorable prognostic sign.

Specific sensitization of the skin is a characteristic feature of some of the granulomatous infectious diseases. Prominent among this group are tuberculosis, brucellosis, tularemia, typhoid fever, coccidioidomycosis, venereal lymphogranuloma and histoplasmosis. The production of so-called sensitizing antibody may be a feature of granulomatous inflammation, but a typical granuloma may evolve without it. Other forms of immune bodies may also be present in these infections. Neutralizing antibodies are conspicuous in the viral and rickettsial diseases; complement-fixing antibody develops in highly significant quantity in syphilis, in coccidioidomycosis and in certain of the parasitic granulomatous infections. Opsonins and

agglutinins as well as precipitins appear in important quantities in brucellosis, typhoid fever and certain other bacterial granulomatous inflammations. The presence of antibodies in the blood serum is not necessary, however, for the development of typical granuloma but tends to suggest a mixed inflammation. Forbus[14] stated that the etiologic diagnosis of inflammatory granulomatous disease presents very great difficulty. From biopsy of the specimen it may be only possible to say that it is a pure granuloma or a necrotizing granuloma.

Ross[16] showed that on injection of staphylococcus toxin into immunized rabbits either a suppurative or a granulomatous inflammation could be produced, depending on the dilution of the toxin; relatively strong toxin produced a suppurative inflammation and relatively weak toxin a granulomatous reaction. There was no sharp demarcation or division between the two reactions, there being a midarea where the reaction partook of both processes.

After intradermal injections of living Staphylococcus aureus into normal animals Cannon and Pacheco[17] found edema of the subcutis with infiltration largely by polymorphonuclear leukocytes. The reaction in skin previously immunized by intradermal injections of killed Staphylococcus aureus was found markedly different. At an early stage there was an enormous infiltration, mostly of lymphocytes and monocytes, in the subcutis. They tended to become massed around a region of marked bacterial concentration, and here there were many evidences of necrosis of the cells of inflammation with accompanying hemorrhage and even thrombosis of the capillaries. These findings suggest that whether the invading microorganism is a toxin producer or not influences strongly the type of cellular defense elicited, and at the same time indicates that in an immunized animal it will require a greater concentration of toxin to produce a polymorphonuclear leukocytic response.

The findings of Cannon and Pacheco[17] may be compared to those of Arkin[18] in periarteritis nodosa, which will be shown later to be a reaction form closely related to granuloma. Arkin divided periarteritis nodosa into four stages. In describing the acute inflammatory stage he noted an infiltration of the media and adventitia of the vessels with polymorphonuclear neutrophils and sometimes also eosinophils, lymphocytes and plasma cells. In the granulomatous

stage he found a marked proliferation of fibroblasts from the adventitia into the inflammatory zone accompanied by a reduction of the polymorphonuclear leukocytes with an increase of the lymphocytes and plasma cells. The histologic picture described by Arkin[18] in cases of periarteritis nodosa is strikingly like that described by Cannon and Pacheco[17] in their studies of the cellular reactions of the skin of the guinea pig, first in the normal animal and then the animal as influenced by local active immunization to intradermal injections of living Staphylococcus aureus.

It would seem to be a reasonable conclusion that the acute inflammatory stage of Arkin[18] takes place before local tissue immunity has reached marked development. After local tissue immunity has reached a high degree the cellular reaction resembles that found by Cannon and Pacheco[17] on injecting Staphylococcus aureus into local areas which had been actively immunized.

Arthus and Breton[19] demonstrated that if an area of skin is sensitized and then antigen is injected into the area a pathologic picture similar to that produced in granuloma will result. Opie[20] observed that when foreign proteins are injected intradermally into rabbits much of the material is quickly demonstrable in the blood stream, but with repeated injection of the antigen the quantity of foreign protein that enters the blood stream diminishes, and finally with advanced immunization none enters unless massive doses have been employed. Furthermore, in the immunized animal the foreign protein is fixed at the site of injection, a fact that Opie felt to be of significance because it was in the immunized area that "anaphylactic" inflammation occurred. This anaphylactic inflammation histologically appears to be indistinguishable from that encountered in pure granulomatous inflammation or from that produced by Cannon and Pacheco[17] by injecting staphylococci into an immunized area of skin.

If this reaction be anaphylactic or allergic, how can it be seen occurring as a part of a normal resistance mechanism such as granulomatous inflammation? If this be the case, "allergy" will have to be redefined to include normal as well as altered reaction. Opie[20] expressed the opinion that since a similar reaction occurs when antigen and antibody are simultaneously injected into the tissues of a normal animal but not when antigen and normal serum are injected, and since the same effect is observed when antigen is injected into

the tissues of a sensitized animal, anaphylactic inflammation occurs when antigen and antibody have met in the tissues.

The only difference between the histologic lesion in the specific granulomatous inflammations, idiopathic granulomatous inflammations and the phenomenon produced in the laboratory and called the Arthus phenomenon is lack of knowledge as to the cause in idiopathic granuloma. In the first, when local tissue immunity is established, a pure granuloma results with or without pronounced central necrosis, depending on the organism involved, or a granuloma of the mixed type results if the organism is capable of some toxin production. In the third the injection of bacterial protein or bacterin which is known to be feebly toxic produces the reaction. The idiopathic granuloma occurs under natural conditions and yet no organism or other source from which nontoxic protein material might be derived has been identified. In this instance only there may be dysfunction (altered reactivity) of some part of the immune mechanism, and logically therefore only an idiopathic granuloma might be termed an allergy.

From the evidence so far presented it would seem that specific granuloma formation with ulceration, if it is near a skin surface, is a normal defense mechanism and should not be termed an allergy, bacterial or otherwise. In the nonspecific or idiopathic granulomas, however, the case is quite different. We have a lesion presenting the clinical and pathologic appearance of a granuloma, in other words, the normal defense mechanism of granulomatous inflammation, but without being able to discover a normal stimulus to initiate such a reaction. The idiopathic granuloma may therefore be considered an abnormal reaction and therefore an allergy. To settle this point it would seem to be necessary to inquire into what is allergy and what is its fundamental pathology.

I shall first outline a hypothesis for allergy that seems to fit all the known facts and yet avoids the paradoxes that had made the subject of allergy and immunology so difficult for me.

ALLERGY

I have found the problems of allergy much less difficult of solution since setting up for myself the following schema.

1. The diagnosis of allergy is primarily clinical. It is on the gross and microscopic appearance of the lesions, not primarily on the basis of immune reactions and hematologic studies, that the diagnosis is made.

2. Allergy is primarily a vasculitis; secondary necrosis, hyaline change and fibrosis are confusing elements in the picture introduced by the attempts of the body to heal the lesion.

3. The vasculitis tends to be focal in character, sometimes involving an entire organ but usually affecting more or less isolated areas (the shock organ).

4. The vasculitis is produced as a result of cell injury that sets free substances such as histamine or the "H substance" suggested by Lewis and co-workers[21-23] or antibody-like substances such as the "necrosin" associated with gamma globulin found by Menkin.[24]

5. The cell injury may take place as a result of an antigen-antibody reaction within the cell or at the cell membrane as suggested by Opie,[20] or it may result from localized vascular spasm causing anoxic conditions in certain areas of tissues which secondarily produce the cell injury resulting in the release of toxic products, as suggested by Müller[25] and Parrisius.[26] Thus clinical appearances typical of allergy may manifest themselves without the intervention of an antigen-antibody type of mechanism.

6. Allergy can be considered as three related but not identical physiologic mechanisms. These mechanisms are to be considered perversions of three normal resistance mechanisms. Considered in the order of their probable phylogenetic and pathogenetic priority they are:

A. Physical Allergy. In this condition physical agents such as cold, heat, fatigue and emotional perturbations produce localized areas of vascular spasms with resulting anoxia, cellular injury and localized vasculitis as demonstrated by Müller[27] and by Brown.[28] Its "immunologic" prototype is that of "homeostasis" as described by Cannon,[29] by which the body adjusts itself to changes in its internal and external environment produced by physical agents.

B. Bacterial Allergy or Tissue Allergy. Focal hyperimmune areas, as suggested by Kahn,[15] attract circulating antigen with re-

sulting cellular injury and vasculitis, producing the clinical picture of allergy. The immunologic prototype is granulomatous inflammation which develops in response to invasion by micro-organisms which are slow or meager producers of toxin.

C. Humoral Allergy. In this form we find the "sensitizing antibody," "blocking antibody," "opsonins," "agglutinins" and the like which appear to be associated with gamma globulin appearing in solution in the blood serum. In this type of allergy sudden, rapid junction of antigen and antibody at the cell membrane or within the cell produces cell injury with the release of toxic products. The vasculitis produced is not so severe as in tissue or bacterial allergy, a fact that suggests that the circulating antibody may have a buffering action and that less toxin is released from tissue cells by reaction. The local allergic lesion has the general appearance of the allergic wheal. Its immunologic prototype is suppurative inflammation with a polymorphonuclear cellular response to invasion by micro-organisms which are potent producers of "exotoxin."

There is nothing in this hypothesis to suggest that these three types of allergy are mutually exclusive; indeed, clinically I feel that they are frequently found occurring in association.

I have found that if one excludes pollinosis and inhalant allergies not more than 10% of allergic patients will be found to give specifically significant cutaneous reactions. In otology and rhinology we are dealing largely with the nonreacting 90%. It should not be surprising, therefore, that our therapeutic efforts directed toward relieving a humoral allergy that is not there should have yielded so little in clinical results. This concept that I have presented vastly broadens the field of therapeutic possibility and has given me considerable success in dealing with previously refractory problems.

Kahn[15] found it unnecessary to conceive that the tissue cells in allergy in man produce "sensitizing" antibodies aimed presumably to render themselves hypersensitive to some antigen or allergen. It seemed to him more reasonable to assume that the antibody produced by an allergic person toward an allergen is essentially not different from the antibody produced toward an antigen or micro-organism. The outstanding disturbance in the allergic person is that his tissue cells respond immunologically to substances that are not antigenic to normal persons; his tissue cells are immunologically hyperactive.

He may react immunologically to drugs or other organic substances and also to inorganic substances; he may react on first contact with an allergic agent in the absence of an incubation period; he may react nonspecifically and most frequently he will give maximal reactions to minimal doses of the allergen.

While Kahn's contribution[15] of the concept of tissue immunity furnishes the key to the puzzle of allergy, the contributions of Müller,[25] Petersen[30] and Selye[31] must also be considered fundamental in the formulation of the concept that I have presented.

I shall review a little of the pertinent literature in regard to this concept of allergy and attempt to show how it connects with the problem of idiopathic granulomatous ulceration under discussion.

In discussing the nature of allergy Rackemann[32] stated that the fact that the symptoms of allergy depend on a characteristic and uniform pathologic condition is important. Spasm of smooth muscle, stimulation of glands and increased permeability of capillaries are produced with such regularity as to justify the concept of a common end product which results from a great number of reactions. He quoted Lewis to the effect that cellular injury results in the liberation of those histamine-like substances which are normal constituents of the cell contents.

In immunity, according to Rackemann,[32] no reaction occurs because the antibodies are predominantly in the circulating blood where they can destroy or modify the antigen before it can make contact with the cells. In the normal person no reaction occurs because there are no antibodies. However, a dose of serum or any foreign substance induces the formation of antibodies which may develop to such concentration as to react with the *remains* of antigen and precipitate a reaction called serum disease. It should be emphasized that serum disease is a normal response of a normal person. Furthermore the differences between this normal response with its ten-day incubation period and acute shock occurring within a few minutes are quantitative rather than qualitative. Antibodies may be many or few; they may be attached to cells or occur free in the blood, or they may be in both situations at the same time. The differences are of degree rather than of kind. Rackemann[32] pointed out that the production of antibodies in general is a normal function, that allergy is a normal function and that allergy is a reaction

which is characterized by the easy formation of cellular antibodies in great abundance. An individual may be considered allergic in the sense that he has an easy tendency to develop hypersensitiveness. In this discussion Rackemann[32] is in agreement with the hypothesis presented in earlier paragraphs, up to a certain point. He states that allergy may result from a great variety of reactions, quotes Lewis to the effect that cellular injury releasing toxic substances from the cell produces the vascular effect resulting in the clinical picture of allergy, yet appears to insist that the only mechanism by which injury to cells can be produced is by the union of antigen and antibody within the cell or at least at the cell membrane. He does, however, appear to be receptive toward the concept that allergy is a normal, not an abnormal mechanism.

Burnet[33] appeared to advance even further toward this position. He stated that the changes which occur in an organism in response to an infection usually enable it to throw off the infection and are thus beneficial. Noninfectious dead micro-organisms may also provoke alteration, and apparently harmless substances may occasionally cause alterations in the tissues or in the circulatory apparatus. He suggested that the basic mechanism consists in the recognition by the tissues of the organism of the difference between "self" and "not self." Identical defense measures in the case of harmless substances such as ragweed pollen may set up a mode of reaction which is actually deleterious to the organism. He can only suppose that on the whole the benefit outweighs the harm, or otherwise the device of immunity-sensitization would not have survived the long course of evolution. All these authors insist, however, that allergy, hypersensitiveness, anaphylaxis and so on are associated with the presence of circulating antibodies.

German immunologists under the leadership of Ehrlich, Pfeiffer and others, being more concerned with the relationship between immunity and serum antibodies, have made us somewhat forgetful of the work of Metchnikoff and his colleagues at the Pasteur Institute who stressed the importance of phagocytosis as a mechanism in immunity.[34] These different approaches to the problem of the resistance of the body to invasion by bacteria led to two concepts of the mechanism involved, the "humoral theory" and the so-called cellular theory of immunity. The belief of Metchnikoff that antibody and complement are derived from leukocytes has received con-

formation from recent workers such as Chase, White and Dougherty[35] and others[36] who have presented convincing evidence that the soluble gamma euglobulin which forms the circulating antibodies comes from the reticulo-endothelial system and probably from the lymphocytes.

Cannon and Pacheco[17] stated that the relatively unsatisfactory results of many years' emphasis on humoral factors in the defense against infectious disease had led to a re-examination of some of the underlying mechanisms involved, and as a result the cellular reactions of immunity were receiving more attention. They stated that accumulating evidence pointed to a close relationship between phagocytic cells, particularly macrophages, and antibody formation. They suggested the concept that antibodies may be merely excess products resulting from ingestion of antigenic substances by phagocytes. Serums or solutions of antibodies may be simply by-products, the fundamental reactions actually occurring within the phagocytic cells. They added that the ability of micro-organisms to adapt, multiply and disseminate may be prevented by the defense mechanisms of the body. These may be both cellular and humoral. The early mobilization of phagocytic cells at the site of bacterial infection may serve to restrain the rapid increase in numbers of bacteria and the rate of engulfment by macrophages may exceed the rate of multiplication of the bacteria. Localization of the organism by mechanical factors such as lymphatic blockade and an antigen-antibody reaction in the tissues may result in the formation of chemotactic substances which quickly lead to a pronounced infiltration by cells of inflammation which are quantitatively and qualitatively different from those responding in the normal animal. In active inflammation it is probable that a summation of all these forces, specific as well as nonspecific, ensures an effective resistance against extension of infection.

The concept of tissue immunity (the third type of immunity) has been extended and developed by Kahn,[15] who has in particular called attention to the defensive properties of the skin and subcutaneous tissues. Kahn stated: "The immunologic significance of the anchoring capability of the cutaneous tissues for micro-organisms and antigen is clear. The cutaneous tissue not only stands guard in preventing micro-organisms and antigens from boring through into the deeper tissues from without but by anchoring micro-organisms

and antigens from within, the same tissue aids the body in eliminating them outwardly. This anchoring capability is not limited to the outer layers of the cutaneous tissue but is manifested also by the subcutaneous tissue. When an antigenic agent is injected into the cutaneous tissue of an immunized individual, it is anchored locally and is circumscribed by an inflammatory reaction. When the same antigenic agent is circulating in the blood stream of an immunized individual, it may similarly be anchored in given areas of the cutaneous tissue and be circumscribed by inflammatory reactions."

Kahn[15] stated that it is reasonable to believe that the injections of foreign protein have similar immunologic effects on a host whether the protein comes from milk, serum, pollens or micro-organisms. He did not feel that it was necessary to call upon the concept of tissue hypersensitiveness to interpret the results observed following the injections of protein into an animal. One can understand, he said, why Richet created the term "anaphylaxis" when he saw an animal die following a second injection of protein directly into the blood stream, and why Arthus believed that he dealt with a condition of local anaphylaxis when he saw local inflammation following a second injection of an antigen given subcutaneously. Such unusual reactions of animals to a second injection, Kahn believed, are readily explicable by assuming not that the tissues have become hypersensitive but that they have become hyperimmune.

Kahn[15] pointed out that studies of the defensive capabilities of antibodies and phagocytes have laid the foundation of present-day immunology, but while these studies have been fruitful in coping with toxin-producing micro-organisms and have thrown light on the role of mobile and fixed phagocytes in infections, as far as the role of the tissues, the very seat of infection, is concerned, little is known. Indeed the mechanism of defense against those micro-organisms which are slow or meager toxin producers and the part played in this defense not only by the tissues but also by the antibodies are as yet an open field for investigation. Studies on tissue immunity, Kahn believed, should also throw light on responses to parasites larger than bacteria. In many cases of parasitism we are dealing with tissue reactions with little indication of any humoral reactions. The mechanism of the tissue reactions to parasites may not differ markedly from the mechanism of these reactions to bacteria and indeed to proteins. Kahn reviewed the development of the

concept of tissue hypersensitiveness and called attention to the fact that the earlier workers such as Richet, Arthus and Breton[19] and von Pirquet[37] combined the phenomenon of local hypersensitiveness or local anaphylaxis with the phenomenon of general anaphylaxis into the concept of "allergy." On the basis of these considerations the sensitized state is generally defined as a condition in which an animal is in some way antagonistic to its own defenses against specific micro-organisms or other antigenic agents. Kahn found himself at a loss to fit this concept of allergy into the scheme of immunity. As an adherent of the "unitarian hypothesis" he believed that precipitins, agglutinins and bacteriolysins represent one type of antibody reacting under different physicochemical conditions. He did not see how it was possible therefore for the same antibody to protect the host under one set of conditions and act as a "sensitizing antibody" under another. He pointed out that many authors regarded allergy as a basically defensive condition by which vital organs were protected at the expense of local injury.

In considering the problems of immunity and allergy from the phylogenetic standpoint, Kahn[15] felt that the defensive mechanisms which a host has developed through evolutionary ages form the bases for the mechanisms he utilizes in freeing himself of protein and other harmless antigens when they are introduced into his tissues. He felt that this view of the relationship between the immunologic responses to micro-organisms under natural conditions and the response to nontoxic antigens under experimental conditions will help greatly in understanding many of the reactions observed in immunity. Kahn felt that in immunity as in other physiologic functions of higher animals, while certain cells have the function of protecting the entire animal against pathogenic micro-organisms, these cells do not carry the entire burden of defense. Rather all cells possess immunologic capabilities to some degree, and it is unnecessary to assume a complete loss of defensive function by all but a certain specialized group of cells, as do the proponents of the concept of humoral immunity. In the struggle for survival the capacity to react against micro-organisms has become inherent in the tissue cells with the result that whenever the tissues come in contact with harmless antigenic material they react as though they were in contact with micro-organisms. This would serve to explain why the same fundamental pathologic picture can be produced by certain

micro-organisms and by the injection of nontoxic foreign protein indifferently. It is to be noted that the organisms producing these reactions under natural conditions usually are of the type that are "slow or meager toxin producers."

Kahn[15] noted that two types of tissue changes can be differentiated as a result of immunization. Interpreted in terms of immune globulin formed by the cells, two types of immune globulin are noted. One type may be looked on as insoluble because it can not be washed away from the cells by surrounding fluids. The other type of immune globulin may be looked on as soluble because it can be washed away from the cells by the surrounding fluids. The former immune globulin is an inseparable part of the cell structure while the latter, finding its way into the fluids of the body, becomes the circulating antibody. Since it would appear that circulating antibodies occur largely in response to toxins and since most of the micro-organisms do not produce a large quantity of soluble toxin, Kahn[15] would seem to imply by this statement that most immunity is not primarily associated with circulating antibody.

He also found that anchoring of micro-organisms and other antigens is the outstanding defense in the immune state. He felt that the widespread prevalence of micro-organisms wherever life exists, and their constant contact with the surface tissues of animals, have produced the localizing mechanisms which are the first step in an elaborate tissue reaction aimed not merely to prevent micro-organisms from invading the body but also to destroy them locally in the area in which they happen to gain entrance. That this anchoring capability should be especially marked in the case of surface tissues can readily be understood. Tissue necrosis in pre-existing inflammatory tissue-antigen reactions Kahn[15] found to be a common immunologic phenomenon. He pointed out that it is seen clinically under natural conditions of infection when the wall which has kept micro-organisms localized in a given focus breaks down, resulting in their escape into the blood stream with a flaring up and necrosis in other pre-existing foci for which cells have become hyperimmunized.

Kahn[15] emphasized, however, that he believed tissue necrosis taking place within an inflammatory area to be a phenomenon which is opposed to the phenomenon of inflammation. The latter phenomenon is a manifestation of a host against a parasite or antigen while the

phenomenon of tissue necrosis, he stated, is a manifestation of a parasite or antigen against the tissues of the host. When an immunized tissue localizes a bacterial antigen, injury to the tissues will produce an inflammatory reaction. If, however, an excess of antigen is present in the localized area, according to Kahn,[15] necrosis will result by an unknown mechanism which he suggested may be blocking of the capillaries by excess antigen.

The disturbances known as allergy in man Kahn believed to be various manifestations of specific hyperimmunity, and he found hyperactivity of a physiologic function to be a common biologic phenomenon. The responses of the allergic person to a particular allergen do not obey the general laws of immunity. In an unimmunized animal only a dose of antigen of a given size will call forth inflammation in the local tissue and a relatively large quantity of the antigen must be present in the blood stream before tissue necrosis in the inflammatory area will become evident. In the allergic person minute doses of the allergen will call forth these phenomena, often nonspecifically.

However, Kahn[15] pointed out the marked difference existing between bacterial and nonbacterial protein as antigen. Taking as an illustration the phenomenon of tissue necrosis in preformed inflammatory areas as exhibited by bacterial-immunized and by protein-immunized animals Kahn found that only an animal in a high state of immunity will exhibit this latter phenomenon, while to a substance such as typhoid vaccine an animal may exhibit necrosis although it may never have received an immunizing injection of this vaccine. It would thus seem evident that the natural immunity to the constituents of the typhoid bacilli corresponds to a marked immunity to a nonbacterial protein and not to a mild immunity to this protein. Kahn did not feel that Pfeiffer's concept that typhoid bacilli contain an endotoxin conforms to newer knowledge. The relatively marked local reactions manifested by man to the injection of typhoid vaccine in the skin and the similarly marked systemic reactions when the vaccine is injected intravenously are due to the immunity possessed by man to the typhoid bacilli and their constituents, and not in his opinion to any endotoxin contained in the bodies of the bacilli.

Kahn[15] divided infectious diseases broadly into three classes: those in which nontoxic antigenic constituents of the micro-organ-

isms play the outstanding roles, those in which toxins of micro-organisms play the outstanding roles and those in which both toxic and nontoxic agents play the outstanding roles in producing the immune responses. It is known that nontoxic protein antigens are capable of producing injury and necrosis of tissue in immunized animals. The phenomenon of tissue necrosis in preformed inflammatory areas is manifested to protein antigens. He believed, therefore, that an infectious disease due to micro-organisms free from exotoxin or endotoxin is entirely possible. He suggested that if we considered a hypothetical infection in which micro-organisms free from toxin play the outstanding role, we would note that any localization of the micro-organisms in a tissue would also lead to local injury followed by inflammation. The host may have been able to bacteriolyze the attacking micro-organisms but this may not mean that he has been able to destroy the liberated constituents of the micro-organisms. Suppose as some protein constituents are circulating in the blood stream and are taken up by the tissues they remain localized in a certain tissue owing to the inability of this tissue to proteolyze them. Kahn had seen repeated instances of the localization of antigen in the tissues of an immunized host in the absence of the capability of such tissue to destroy it. As time goes on, he supposed, the patient becomes re-infected with similar micro-organisms. Recalling the phenomenon of tissue necrosis in pre-existing inflammatory areas we might expect the appearance of a granuloma with central necrosis in such an area of tissue.

Kahn[15] pointed out that keeping in mind the complexity of infective processes in which nontoxic bacterial constituents act as antigens, a single abnormality in the immunologic chain which might interfere with the bacteriolysis of the micro-organisms, with the proteolysis of the protein constituents or with the destruction of all other antigenic constituents may lead to tissue disturbances. It must also be kept in mind, he said, that the phenomenon of tissue necrosis may manifest itself only to a slight degree, resulting in minor tissue disturbances. Hence any localization of a nontoxic antigen in a tissue which might be insufficient to produce noticeable disturbance under ordinary circumstances might give indications of disturbance when the same or some similar antigen is circulating in the blood stream, since this circulatory antigen would also tend to accumulate in the same tissue. He was inclined to believe that when we meet

with disturbances that tend to come and go, the causative agent is a nontoxic antigen, and the flare-up represents in most instances a manifestation of the phenomenon of tissue necrosis in preformed inflammatory areas.

Kahn[15] here presented a hypothetical case which almost exactly fits the findings in a lethal granulomatous ulceration in the midline tissues of the face. Through previous infections these naturally reactive tissues might have become hyperimmunized or might still retain nontoxic antigen. Tissue necrosis might then ensue from any specific or nonspecific nontoxic antigen circulating in the blood, possibly even from absorption of "anaphylactogens" through the intestinal wall. The hypothesis would also serve to explain the fundamental histologic identity of the process with granulomas in the same area caused by any of the micro-organisms which are meager toxin producers.

Although the concept of tissue immunity as outlined by Kahn[15] is not accepted by all immunologists, its development appears to have been made along logical lines and it integrates and makes understandable much that is admittedly confusing when the process is considered along the lines of immunity versus hypersensitivity or allergy. In addition, since 1936 when Kahn's book, "Tissue Immunity," was published, no evidence appears to have been produced which would indicate his hypothesis to be incorrect. In discussing "Immunity Versus Hypersensitivity" Boyd[38] gave no better explanation than that of Burnet[33] already mentioned in this paper. Boyd[38] himself stated, "Possibly almost any kind of body cell can produce some antibodies for local concentrations have been observed." According to Landsteiner,[39] findings which suggest the possibility of local antibody formation in infected sites have been presented by Osterkov and Anderson, Tapley and associates, Sachs, Burnet, Siegal and associates and Cannon and associates. From the viewpoint of phylogeny, Kahn's hypothesis seems highly probable.

Smith and Martin[34] pointed out that the phenomenon of bacterial allergy is entirely different from that of anaphylaxis. The reaction following the introduction of the antigen into an animal with the bacterial type of hypersensitivity does not appear until many hours after the injection is made. The hypersensitivity cannot

be transferred passively to another animal by the injection of serum from a hypersensitive animal, and if tissue cultures are prepared from animals with the bacterial type of sensitivity, exposure to the antigen will result in death of the cells of the tissue culture. In anaphylaxis a characteristic response is displayed by each animal species and some species are exceedingly difficult to sensitize and shock. Bacterial hypersensitivity on the other hand can be produced in almost any animal and there are no outstanding differences in the reactions obtained in different species of animals. The bacterial type of hypersensitivity as a rule follows the introduction of the antigen into an area of inflammation, which under natural conditions means infection. Smith and Martin[34] feel that in spite of the failure to demonstrate antibodies in the serums of animals with bacterial sensitivity it is the consensus of most investigators in the field that bacterial hypersensitivity is a true antigen-antibody reaction. The antibodies, however, appear firmly attached to the tissue cells and do not occur in sufficient amounts in the circulation to be detectable by any method developed at the present time. That antibodies must appear in the blood at some time is, Smith and Martin[34] feel, suggested by the fact that the tissues all over the body become hypersensitive and a reaction will occur to the injection of the antigen at any site. They also pointed out that Chase has transferred sensitivity to tuberculin from sensitized to normal guinea pigs by the injection of leukocytes from pleural exudates.

The description of bacterial allergy presented by Smith and Martin[34] correlates very closely with the picture of granulomatous inflammation presented by Forbus.[14] This suggests that there are real differences between the defense mechanism of granulomatous inflammation and that of suppurative inflammation although there is a fundamental, rather close relationship.

In discussing the modern concept of inflammation, Menkin[24] stated that inflammation is a manifestation of severe cellular injury in higher forms. As such, the inflammatory reaction requires the presence of vascular and lymphatic structures as well as tissue cells. The reaction, which is initiated by a disturbance in fluid exchange manifested primarily by an increase in capillary permeability, tends to be stereo-patterned. Close scrutiny reveals throughout a fundamental pattern which is largely referable to various basic common

denominators or biochemical units liberated by injured cells irrespective of the nature of the stimulating irritant. The initial increased capillary permeability and the early migration of polymorphonuclear cells are primarily caused by a polypeptide to which there may be attached a prosthetic group called leukotaxine. Leukotaxine has no similarity to histamine and has no relation to the H substance of Lewis. Leukotaxine fails to alter the number of circulating leukocytes when administered intravenously.

A leukocytosis promoting factor (L. P. F.) is liberated by injured cells and can in turn be recovered from exudates. The factor is thermolabile and nondiffusible. It can be extracted in the pseudoglobulin fraction of exudates, and cataphoretic studies suggest its association with alpha[1] and alpha[2] (α^1 and α^2) globulins of exudates. L. P. F. promotes a discharge into the circulation of immature granulocytes. It is present in human exudate but is absent from normal blood serum.

Menkin[24] found that there is also liberated by injured cells a toxic substance called "necrosin" which either is a euglobulin or is associated with the fraction in exudates. Its cutaneous injection is followed by swelling, redness, varying degrees of central necrosis, lymphatic blockade, injury to the endothelial walls of the blood vessels and swelling of collagenous bundles. Necrosin is absent from normal blood serum, but it may be recovered from the serum of an animal with inflammation.

The whole euglobulin fraction of exudates not only induces a conspicuous degree of cellular damage but also causes both a rise in temperature and a marked drop in the leukocyte count—a state of leukopenia. The fever producing factor can be separated from the true euglobulin by a method of differential solubility. This pyogenic factor has been termed "pyrexin." It is thermostable. Its action is probably central, for pentobarbital sodium (nembutal) and antipyretics tend to reduce its effect. The leukopenic factor of exudate seems closely associated with pyrexin. The presence of such a factor in exudative material, particularly if the exudate is at an acid pH, may be of help in explaining the leukopenia attending numerous inflammatory processes. Pyrexin in exudates liberated by injured cells opposes the L. P. F. in its mode of action. The level of leuko-

cytes in the circulation may be the resultant of these two opposing tendencies.

This work of Menkin[24] seems to supplement the hypothesis of tissue immunity presented by Kahn.[15] These substances in the cell, released by injury, might be considered to be some of the nonspecific natural antibodies to which Kahn[15] referred. The liberation of necrosin, with the production of a lymphatic and capillary blockade, seems a better explanation for tissue necrosis than Kahn's admittedly halting suggestion[15] of lymphatics and capillaries blocked by bacterial antigen in excess. This does suggest, however, that contrary to Kahn,[15] necrosis is also a defense mechanism concerned with the localization of bacteria or bacterial antigen. Nothing in Menkin's work[24] denies the possibility of the development of antibodies by the cell, or the ability of cells under certain conditions to fix bacterial antigen and react to subsequent antigen circulating in the blood serum with cell damage and tissue necrosis.

Liberation of necrosin without the L. P. F. might explain why in lethal granulomatous ulceration of the nose and pharynx there is so often fever without the expected increase in leukocytes or change in the differential count.

This review suggests that altered reactivity in the defense mechanism can produce at least two types of allergy. The one, encountered especially in pollinosis and inhalant allergies, is associated with humoral antibodies; the other, encountered in idiopathic granuloma, is not necessarily associated with circulating antibody but is primarily associated with the development of hyperimmune areas in the body. These two types of reactivity are not mutually exclusive but may be combined.

The answers to the first and second questions proposed seem to give little difficulty. Granuloma formation is the body's method of resistance to certain preferred stimuli; the midline tissues of the face frequently are involved because in this region localized areas of immune cells tend to develop.

THE PATHOGENESIS OF IDIOPATHIC GRANULOMA

Teilum[40] has reviewed the literature on nonspecific granulomas and diseases related to them. He stated that by looking on these lesions from a common pathogenetic viewpoint based on morphologic

observations and experimental studies on the vascular and tissue changes in allergy, by Gruber,[41] Jäger[42] and Rössle,[43] essential support has been obtained for the concept that these lesions are primarily vascular and are of allergic nature. It ought to be expected, therefore, that the physiologic mechanism would be similar in all cases, owing to a particular way of reacting to various agents of infectious toxic nature.

According to Klinge,[44] the essential morphologic substrate of these related conditions is a swelling of the ground substance (collagen) of the connective tissue. This applies to the blood vessels which are involved in the process, with edema, fibrinoid degeneration and swelling of the collagen fibrils in all the layers of the walls of the vessels as the first morphologic change. The fibrinoid swelling (necrosis) of the ground substances is interpreted as an increase in the toxic damage that otherwise manifests itself as diffuse edematous swelling. Klinge[44] believed nonspecific granuloma to be an allergic lesion which pathogenetically is closely related to rheumatic fever as well as to allergic vascular lesions such as periarteritis nodosa and lupus erythematosus disseminatus. Therefore he felt that the necrotizing inflammatory processes in the connective tissues around the larynx and so forth are pathogenetically of quite the same character as the areas of necrosis in lungs and lymph nodes found in other vascular lesions of an allergic character and that they signify an allergic tissue reaction. Corresponding necrotic processes may occur in various organs.

It is of interest in this regard that Wegener[45] observed periarteritis nodosa to be a common finding in patients with lethal granulomatous ulceration. He felt that the condition causing the granuloma and that causing the periarteritis nodosa might be the same. He also pointed out that periarteritis nodosa was found in virus diseases and in rickettsial disorders and offered the suggestion that a viral invasion might be responsible for lethal granuloma. Gerlach[46] in addition described necrosis of arterioles at the site of the Arthus phenomenon (and the observation has been confirmed repeatedly). Periarteritis nodosa therefore would seem to be the same necrotic vascular reaction appearing in somewhat larger vessels that causes the Arthus phenomenon when it involved capillaries.

Weinberg,[47] in discussing periarteritis nodosa in granulomas of the type (idiopathic) considered in this paper, stated that the strik-

ing feature of the cases which have been studied thoroughly and fully reported is that they all present a history of long-standing upper respiratory infection with the development of ulcerations of the nose, mouth and trachea and with final development of the picture of periarteritis nodosa. He felt that the problem resolved itself into the explanation of the granulomas and their relationship to the periarteritis nodosa. Although iodism, glanders, tularemia, leprosy, rhinoscleroma, blastomycosis and sporotrichosis all give a somewhat similar histologic picture, Weinberg[47] could not demonstrate the etiologic agent in each of these diseases in the cases he studied and he could not obtain a history of related exposure. He considered the possibility that a virus might be the causative agent, but he stated that of the viruses only that of veneral lymphogranuloma produces a microscopic picture which is conceivably similar. He felt, therefore, that we are left with a picture which clinically consists of ulcerations of the upper respiratory tract associated with evidence of focal alterations in the lungs and anatomically shows multiple granulomas of unknown origin, involving one or more organs with terminal development of periarteritis nodosa. Weinberg[47] felt that the constancy of the history of antecedent chronic infection in these cases lends support to the belief that hypersensitivity may be a factor in their development.

In histologic study of material from four asthmatic patients who died, Harkavy[48] found that the chief pathologic changes responsible for the granulomas and periarteritis present were due to varying degrees of hyperergic and anergic vascular reactions in the tissues involved.

Rich and Follis[49] found that an Arthus phenomenon could not be produced in a tissue devoid of blood vessels. These investigators caused capillaries to grow into the cornea of one eye of sensitized rabbits. A small drop of the foreign serum to which the animal was sensitized was injected into the cornea at a short distance from the capillaries. A similar injection was made into the cornea of the opposite, nonvascularized eye and into the vascularized cornea of normal control animals. An Arthus type of reaction occurred in the vascularized cornea of the sensitized rabbits but not in the nonvascularized eye, nor in the vascularized eye of the control animals.

It would seem, therefore, that evidence is at hand which suggests that one of the fundamental resistance mechanisms of the animal is a typical localized cellular immune response, primarily vascular, resulting in "the Arthus phenomenon" when capillaries are involved, producing a granuloma in deeper tissues or a granulomatous ulceration if skin and subcutaneous tissues are involved. The granulomatous ulceration has a certain tendency to occur in the midline of the face, but is by no means confined to this location. There seems to be a certain tendency for the involvement of the larger vessels (periarteritis nodosa) to occur toward the end stages of the disease. The end stages of the disease also seem to be associated with marked lethargy and weakness on the part of the patient (addisonoid symptoms). The lesions produced by microorganisms are clinically and fundamentally identical with the idiopathic lesions. Therefore if "allergy" is the cause of the nonspecific lesions, it would seem logical that such "allergy" is a dysfunction of the immune mechanism that normally produces granulomas.

Rich and Gregory[50] reported an experimental demonstration that purported to show that periarteritis nodosa is a manifestation of hypersensitivity. They stated that in their study periarteritis nodosa had been reproduced in all of its essential details in the experimental animal by creating conditions similar to those obtaining in serum sickness in the human being. They stated, "The demonstration that periarteritis nodosa is a manifestation of anaphylactic hypersensitivity is in line with the long recognized fact that the blood vessels are susceptible to anaphylactic injury." They pointed out that the anaphylactic wheal is in itself a result of capillary damage produced by increased sensitivity and the Arthus phenomenon is clear evidence of a more marked vascular injury. They reported that after a single large injection of serum their animals developed the capacity to react to the small intracutaneous test dose of 0.1 cc. of serum with large persisting lesions which in 5 of 14 animals were hemorrhagic and in 4 were necrotic or examples of the Arthus phenomenon. This is additional evidence that the same physiologic mechanism produces the lesions in both periarteritis nodosa and granulomatous ulcerations.

In discussing the pathology of sulfonamide allergy in man, More, McMillan and Duff[51] stated that the fundamental pathologic change that is elicited by the allergic reaction is not apparent be-

cause there is no evidence that any single tissue is the primary reactant. Basically all the lesions are a complex of tissue destruction and of proliferation of the reticulo-endothelial cells in the affected area. They could not determine whether necrosis or reticulo-endothelial activity was the cause or effect of the reaction.

Boyd[52] stated that he had encountered a case of disseminated lupus erythematosus with very characteristic collagenous degeneration in the glomerular tufts and also in the vessels of the lungs. In association with these changes in the lungs there were beautiful granulomas extremely like sarcoid lesions. These were situated in relation to arteries.

Duff[53] reported the study of 22 cases in which necropsy was performed and in which the patient had received sulfonamides during life. These cases showed either a granulomatous lesion (13 cases) or acute necrotizing arteritis (7 cases) or both lesions in common. Duff[53] felt that the granulomatous lesions and the necrotizing arteritis were closely comparable with periarteritis nodosa. He stated that whatever may be regarded as the etiology or pathogenesis of these lesions, the evidence gave strong support to the idea that the granulomatous reaction encountered in some cases of periarteritis nodosa belongs to the same disease or rather is a part of that disease. He felt that his observations supported the view that all of these lesions are of "allergic" nature.

Weinberg[54] objected to the concept that the "allergy" present in such cases was to sulfonamides. He pointed out that cases showing the same granulomatous reaction with particular involvement of the lungs and upper part of the respiratory tract and associated with periarteritis nodosa have been reported in the literature as far back as 1906. Furthermore the patients on whom Wegener reported in 1939 did not receive any sulfonamide drug therapy.

From the evidence presented, which is very convincing, we should be able to consider granulomatous formation and periarteritis nodosa as essentially the same condition and apply evidence dealing with either, indifferently, to both.

Selye and Pentz[55] presented evidence that in man periarteritis nodosa can be the consequence of exposure to a variety of nonspecific damaging agents. Even in experiments on animals it was pos-

sible to reproduce the conditions by mere exposure to such nonspecific damage as cold. Periarteritis nodosa has been produced experimentally by Selye[31] by overdosage with the adrenotropic hormone of the anterior lobe of the pituitary or hormones of the adrenal cortex. It has been claimed that the vascular changes produced by chronic overdosage with desoxycorticosterone are secondary to the hypopotassemia induced by this compound. Selye[31] disagreed with this view, since the giving of excess potassium failed to protect against these lesions in animals receiving excessive amounts of desoxycorticosterone. It appeared more probable to him that the salt-active corticoids produce such changes by virtue of their sodium-retaining property. This interesting observation recalls to mind that many authors have suggested that a tendency toward allergy (hypersensitivity-hyperimmunity) is promoted by the sodium ion. Selye[31] has found that in conditions of long-continued stress, such as are present in nonspecific granulomatous ulcerations of the midline tissues of the face, the hypophysis produces increased amounts of corticotrophic hormones. Selye suggested the possibility that through alterations in the corticotropic hormones or in adrenal cortical responses any type of alarming stimulus may cause a condition of "relative adrenal cortical insufficiency," in which there is an increase in the production of the sodium-retaining corticosterones such as desoxycorticosterone at the expense of those corticoids which favor excretion of sodium ion and utilization of sugar, such as 17-hydroxy-11-dehydrocorticosterone. Selye[31] has also found evidence which makes it appear very likely that the initial acidosis of the shock phase of the alarm reaction is reversed during the countershock phase.

Petersen[30] has offered evidence that a relative alkalosis favors arteriolar and capillary constriction. Müller[24, 25] Parrisius,[26] Brown[28] and others have found that a spastic state of the arterioles is associated with allergic conditions. Selye has also found evidence that the alarm reaction may have an important effect on serologic immune reactions. He has shown that the increased production of adrenal corticoids is followed by destruction of lymphocytes. Chase, White and Dougherty[35] and others have offered very convincing evidence that the lymphocyte is probably the principal source of gamma globulin, from which the antibodies appear to be formed. It would therefore seem probable that the humoral anti-

bodies depend for their release on production of hormones of the adrenal cortex. It would not be surprising to find that these hormones played a part in the mechanism by which such antibodies are formed, and that "allergy" or hyperimmunity is concerned with changes in the activity of the adrenal hormones. A relative increase in the salt-retaining hormones and a relative decrease in the "antagonistic" hormones favoring secretion of sodium according to Selye appear to produce other conditions known to be associated with allergy. Beckman[56] and others have pointed out that increasing relative acidity of the body will tend to relieve allergic conditions. It would seem, therefore, according to Selye's[31] hypothesis that in "allergy" we have a dysfunction of the alarm phase of the general adaptation mechanism rather than dysfunction of a specific mechanism having to do only with the adaptation of the body to the presence of micro-organisms. It is also obvious that the cell injury which releases the substance from the cells need not be by intervention of a toxin-antitoxin mechanism. Cell injury may be produced by the anoxia secondary to physical and emotional stimuli in unstable individuals. This type of cell injury can produce all the clinical features known as allergy.

To recapitulate, "lethal granulomatous ulceration of the nose, pharynx and larynx" appears by preference in that region because this is a region made up of large areas of skin and subcutaneous tissue in juxtaposition with mucous membrane and submucous tissue. Such tissues have an innate capacity to develop hyperimmunity, possibly greater than any other area of the body.[15] Tissue immunity is from the phylogenetic standpoint the most primitive form of resistance to invasion by micro-organisms. The body tends to respond to invasion by micro-organisms which are meager producers of toxin by a stereotyped reaction in which the earlier aggregation of leukocytes is replaced by plasma cells and macrophages as local immunity develops. This is accompanied by a "capillary and lymphatic blockade" with the formation of central necrosis caused by cutting off the blood supply. This is essentially the Arthus phenomenon. Associated with the production of central necrosis is the production of areas of panarteritis in some of the smaller and larger arterioles. This is essentially periarteritis nodosa. It is presumed that the same mechanism working in different sized vessels produces both phenomena. It has been shown that both the Arthus phenomenon and periarteritis nodosa can be produced in experi-

mental animals by injection of nontoxic protein (anaphylactogen). It has been stated that idiopathic granulomatous ulceration and periarteritis nodosa together with rheumatism, Libman-Sachs syndrome, lupus erythematosus and other related conditions are instances of vascular bacterial "allergy."

Kahn,[15] however, has suggested that the reacting areas are areas of tissue hyperimmunity where antibodies formed from insoluble globulins are in excess. At a subsequent infection these areas will extract antigens, specific or nonspecific, circulating in the blood and localize them in the area with production of the necrotizing and granulomatous vascular phenomena. Kahn suggested that allergic individuals are those who develop tissue immunity to substances to which normal individuals do not become immunized, develop higher degrees of immunity and develop it more readily than normal individuals. Kahn does not feel that the concept that all resistance to invasion of the body by micro-organisms has been taken over by certain specialized cells of the reticulo-endothelial system is tenable. Kahn's hypothesis explains the development of the Arthus phenomenon when the body is invaded by micro-organisms which produce little if any toxin and also how this phenomenon might appear in the absence of specific infection in a hyperimmune individual by activation of highly immunized areas of tissue by nonspecific, nontoxic proteins gaining entrance to the blood stream. Menkin[24] has found that damaged tissue cells release a substance associated with gamma globulin, necrosin, which is capable of producing the central necrosis which Kahn did not adequately explain.

Selye,[31] however, presented evidence to indicate that periarteritis nodosa could also be produced by exposing an animal to such damaging stimuli as cold, fatigue or emotional perturbation. This effect was produced by stimulation of the adrenotropic hormone of the anterior pituitary which in turn stimulated the production of hormones of the adrenal cortex. He found evidence which suggested to him that such stimulation caused a relative adrenal cortical insufficiency with excessive production of the salt-active hormones such as desoxycorticosterone and decrease in the "antagonistic" hormones such as 17-hydroxy-11-dehydrocorticosterone, as well as a decrease in the pituitary growth hormone, prolactin and gonadotropic hormones. During the period of excessive secretion even dur-

ing the stage of exhaustion, the adrenal cortex is enlarged. Associated with these adrenal changes are changes in fluid and electrolyte metabolism (which are controlled by hormones of the adrenal cortex) with a rise in the pH, a retention of sodium ion in extracellular fluid, a tendency toward vasoconstriction with the production of localized tissue anoxia, conditions which have been long associated with "allergy." It therefore seems reasonable to assume that tissue immunity is a phase of the general adaptation mechanism, and that hyperimmunity or bacterial allergy occurs in individuals who have a tendency toward relative adrenal cortical dysfunction. "Allergy" in this case would have to be defined in the very broadest terms and the tendency to limit it to disorders of humoral immunity would have to be completely ignored.

Under this hypothesis an individual with lethal nonspecific granulomatous ulceration of the nose, pharynx and larynx would be considered one who suffered from a relative pituitary or adrenal cortical dysfunction.

Selye[31] has indicated that periarteritis nodosa tends to develop more readily in the presence of high-sodium content of the body fluids but that even with such high-sodium content, acidifying salts such as ammonium chloride will tend to prevent the development of periarteritis nodosa.

Selye[31] has suggested that in animals under prolonged overdosage of desoxycorticosterone a great tendency toward fatal hypoglycemia develops. Under the influence of prolonged alarming stimulation, such as would be provided by a lethal granuloma according to Selye's hypothesis, the same condition should be expected. In lethal granuloma the extreme weakness and lethargy of these patients are noteworthy and several authors have referred to their "addisonoid" symptoms.

Since Selye[31] has suggested that under certain conditions of strain the adrenal cortex may produce disproportionate and excessive amounts of salt-active corticoids with a relative deficiency of sugar-active corticoids, these effects could probably best be counteracted by the giving of adequate doses of such a substance as 17-hydroxy-11-dehydrocorticosterone, which is known to counteract some of the malign effects of overdosage of desoxycorticosterone. Selye stated that if resistance were dependent to any great extent upon increased

corticoid hormone production, treatment with corticoids should have given more satisfactory results than have so far been obtained. In this connection he pointed out, however, that it is of interest to note that even the basic corticoid hormone production of the adrenal is apparently enormous in comparison with the amount of corticoid substance that has been administered for therapeutic purposes. Thus bio-assays performed on the venous blood of adrenal glands indicate that "the average output of one suprarenal gland per minute per kgm. body weight was equivalent to 0.6 gm. of suprarenal tissue." "The potency of 1 ml. suprarenal plasma was at least several times, occasionally 10-12 times, as high as the activity obtained by extracting 1 gram of gland."

There is very convincing evidence, Selye[31] felt, that in combating damage during the alarm reaction the sugar-active corticoids are effective, but there is doubt whether the salt-active corticoids which are readily available commercially are of any value. Since commercial preparations of sugar-active corticoids are often impure and not available, it is not surprising that up to the present it has rarely been possible to improve markedly upon the natural performance of the adrenal cortex. It would seem, therefore, that to test the curative effect of this hypothesis in lethal granuloma we must wait for better or greater production of the necessary hormones.

The unanswered questions are answered in the review of the literature.

First, the occurrence of granulomatous inflammation without an adequate normal stimulus can be considered a type of allergy. Second, this dysfunction appears to rest on a disorder of the secretion of 17-hydroxy-11-dehydrocorticosterone (compound "E" of Kendall) and the disorder is fundamental in producing all the dysfunctions, such as relative alkalosis, relative anoxia, capillary permeability and so forth, that are considered to be characteristic of the allergic state.

REPORT OF CASES

CASE 1.—A woman, 48 years of age, gave the history that about three and one-half years previous to her visit to the clinic ulcerations of the mouth which were cyclic in character had begun to develop. They would appear every six months and last for three months; the patient had felt very well in the intervals. She lost weight and strength with each attack but recovered between times. On several occasions she had received penicillin for a few days with apparent benefit.

About a year after the ulcers in the mouth first appeared, a yellow-green purulent discharge from both sides of the nose developed. The patient stated that some type of intranasal operation had been done in January of that year without any evident influence on the symptoms. During the following year she had received penicillin and sulfonamides at irregular intervals and felt relatively well during this entire time. In February of the ensuing year, however, there had been a marked increase in the nasal discharge and recurrence of the sores in the mouth which extended posteriorly, producing considerable pain on swallowing. Treatment at home no longer helped. She had been hospitalized and received penicillin for eight days and a sulfonamide for three days without any particular effect on the lesions. In June of that year hoarseness had developed and the left eye had become red and inflamed. About the same time red, swollen and painful gums developed and two weeks later a red crusted lesion about the size of a five-cent piece appeared on the right shin and a little later several others on the same leg, and a subcutaneous nodule was found on the left thigh. A month later an ulcerated lesion about the size of a nickel developed on the dorsum of the right forearm and a subcutaneous nodule on the flexor surface of the left forearm. There was no bullous formation preceding the appearance of these lesions and there had never been a purulent character to the discharge from them. From the first there had been nothing but the development of a dry leathery crust with no pain or secretion. The general symptoms of anorexia, fatigue, loss of weight and a feeling of fever developed.

On examination in the Section on Otolaryngology and Rhinology the nasal septum was found thickened on the left by a granulomatous-appearing ulceration which was covered by a tenacious yellowish exudate. Attempts to remove the exudate resulted in bleeding. The nasal mucosa was pale and swollen and had a peculiar granular appearance. On examination of the mouth the gingivae were found to be swollen and congested. There was a superficial ulceration on the left side of the tip of the tongue and there was a ragged, shallow ulceration involving the soft palate, the uvula and the posterior pharyngeal wall. The base of the ulcerated area was covered with a tenacious, yellowish gray exudate. The entire larynx had an edematous appearance, especially marked in the epiglottic folds. The vocal cords, while a little thickened, appeared relatively normal.

Of three consultants in the Section on Otolaryngology and Rhinology who examined the patient on admission, one felt the lesion represented Boeck's sarcoid, one thought it might be either Boeck's sarcoid or tuberculoma but felt that serologic tests for syphilis should be checked carefully and the third felt that the lesion was unquestionably tuberculosis.

Examination of the eyes was reported to show a possible scleritis of the left eye. Fields were roughly negative. Fundus examination showed the retinal arterioles to be slightly narrowed with a few hyaline spots in the choroid on the right.

General physical examination showed a slightly emaciated woman having a five-cent-sized discrete, crusted, depressed erythematous lesion on the dorsum of the right forearm. There was a similar erythematous macule on the right shin and a smaller lesion near the right knee. There were several pea-sized crusted macules on the left thigh. There was a slightly tender, firm, subcutaneous nodule posterior to the left ankle and a tender, erythematous nodule under the skin of the flexor surface of the left forearm.

The dermatologic consultant who saw these lesions felt that the differential diagnosis lay between an "id" reaction from the granulomatous lesions in the mouth and pharynx, a deep mycosis such as coccidioidomycosis, histoplasmosis or moniliasis, papulonecrotic tuberculid, atypical pemphigus or erythema nodosum with the possibility of lymphoblastoma to be considered also.

A specimen for biopsy was taken from the lesion on the left side of the nasal septum and was reported to be "inflammatory tissue." A second specimen was immediately taken and reported to be "very inflammatory tissue." Nothing suggestive of tuberculosis, fungous infection, protozoan infection or a malignant lesion was seen. The results of examination of the sputum were negative for acid-fast bacilli and a roentgenogram of the thorax was reported to be negative except for the presence of bilateral calcified hilar nodes. The patient was seen by a consultant from the Section on Bacteriology who took scrapings of the tissue for culture and smear and a specimen for biopsy from the lesions of the nose, palate and pharynx. Several smears were negative for acid-fast bacilli. Cultures were found positive for Staphylococcus aureus and Neisseria catarrhalis. The specimens for biopsy from the nose and throat were positive for Staphylococcus aureus (great numbers). A peculiar feature reported was the diffusion of the staphylococci through the tissues without any apparent effort on the part of the body to limit their advance. The growth of these staphylococci was completely inhibited by 0.1 unit of penicillin per ml. and by 6 micrograms of streptomycin per ml.

Study of the blood revealed 4,040,000 erythrocytes and between 3,000 and 5,000 leukocytes per cmm. The concentration of hemoglobin was reported to be 12.7 gm. per 100 cc. Differential count showed 25% lymphocytes, 3% monocytes, 70% basophils. A smear of the blood was reported to show toxic polymorphonuclear leukocytosis with a fairly well marked left shift. There was some hypochromasia. Nothing diagnostic was seen. Bleeding time was reported to be 5 minutes and coagulation time 4 minutes and 30 seconds. Prothrombin time was reported to be 23 seconds. Sedimentation rate by the Westergren method was found to be 43 mm. per hour. The results of Kline, Kahn, Hinton and Wassermann tests were reported negative. A roentgenogram of the sinuses was reported to reveal thickened membrane in all the sinuses.

It was therefore decided on the basis of these findings that we were dealing with a nonspecific granuloma of the type seen in gangosa but that the staphylococci might be playing a part.

A consultant in antibiotic therapy saw the patient, reviewed the findings and advised giving 1,000,000 units of penicillin daily by continuous intravenous drip for a minimum of three weeks. The patient was hospitalized and the therapy was started. The third day the patient's temperature rose to a peak of 102° F. and after this she had a daily remittent fever with peaks of between 103° and 105° F. throughout the remainder of her course in the hospital. Daily leukocyte counts showed from 5,000 to 8,000 cells per cmm. with a normal differential count on smear. In fact the number or percentage of the different white blood cells did not vary throughout the patient's illness and showed little evidence that the patient was suffering from a serious disease.

At the end of three weeks of penicillin therapy little change could be seen in the appearance of the lesion or in the patient's condition. The consultant in

clinical bacteriology again saw the patient and again took smears and specimens for biopsy from the pharynx and larynx. At this time cultures were found negative for staphylococci but there were many colonies of Candida (Monilia) albicans present. The biopsy showed these organisms to be infiltrating between the tissue cells in the same uninhibited manner that the staphylococci had been seen to do in the previous biopsy, performed before penicillin was given.

It was then decided to try the effect of transfusions. Eleven transfusions of 500 cc. of whole blood were given at intervals of ten days. At the same time vitamin K, liver extract with copper and iron, and capsules containing several times the known minimal daily dose of the several vitamins were given daily. For a week folic acid was also given daily. These treatments did not affect the patient's local condition and during this time several subcutaneous nodules and dry necrotic ulcerations of the skin on the legs and arms developed. Blood cultures were repeatedly negative. A swelling of the right leg to the groin with tender red lumps under the skin developed.

A consultant in vascular disease who was called in felt that there might be a thrombosis of the right femoral vein, but the red, round tender areas, chiefly in the upper mesial region of the thigh, felt more like erythema nodosum than phlebitis. He felt that he could not differentiate satisfactorily between deep venous thrombosis and a superficial lesion with edema. He suggested the possibility that periarteritis nodosa might be present and asked that a biopsy of one of the tender nodules be done.

Another consultant in internal medicine, who was called in, expressed the opinion that the patient had infection with histoplasma capsulatum. He felt that this hypothesis would account for all the symptoms and signs, especially the lack of response to penicillin. He felt that the cutaneous and mucosal lesions, the fever and the systemic manifestations all fitted very well. He pointed out that biopsies of skin and mucous membrane and even the results of cutaneous tests may be negative, and the exact diagnosis may be impossible to make except postmortem.

The dermatologic consultant agreed that histoplasmosis was a most probable diagnosis, but protested that in spite of repeated search for organisms on repeated specimens he had been unable to find the organism. The patient consented to another biopsy and a portion of tissue was sent to the consultant on clinical bacteriology, another to the consultant on clinical mycology and a third to the dermatologic pathologist. Cutaneous tests for histoplasmin and coccidioidin were repeated and the results were negative. Tissue from the pharynx and forearm was reported negative for acid-fast bacilli and fungi by the mycologist, the bacteriologist reported smears and cultures negative except for a few colonies of Candida albicans and the pathologist reported tissue from the pharynx to be a "granuloma," the tissue from the right forearm to show a nonspecific subacute granuloma with necrosis and the lesion from the left arm to be lupus erythematosus. Evidence of periarteritis nodosa could not be found.

In view of the possibility of the disorder being histoplasmosis, 6 gm. of sulfadiazine daily in divided doses was given for 21 days. Since this appeared to have no effect on the progress of the disease, 2 gm. of streptomycin daily was given for 17 days, also without apparent effect.

A consultant in hematology was then asked to see the patient. He felt that the hypertrophy of the upper gums with increase in the interdental tissues re-

sembled that commonly seen in monocytic leukemia. He did two sternal aspirations. He found numerous units variable in size, all floating in the fixing solution. Nothing abnormal was found. He made the comment, "This is pretty good looking bone marrow, and I can find nothing helpful." He suggested, however, that the patient be treated with roentgen therapy as though the case were one of monocytic leukemia. This was done. After the roentgen therapy the patient reported subjective improvement but there was no observable improvement in the lesions present.

The temperature began to rise to peaks of 104° and 105° F. daily. Blood and urine cultures taken at the peaks of fever were repeatedly negative. The results of inoculations of guinea pigs done when the patient was first admitted were reported negative. The dry, necrotic cutaneous lesions began to increase in number, pleuritic pains in the thorax developed, the lesions in the palate and pharynx became more necrotic and the soft palate split in half.

The consultant in clinical pathology saw the patient again and took numerous cultures and smears. All cultures showed a pure, heavy growth of Staphylococcus aureus. No anaerobes were found. He stated that the staphylococci found were resistant to penicillin, requiring 15 units per cc. to cause inhibition of growth. They were also quite resistant to streptomycin, requiring 6 to 12 units per cc. to inhibit growth. Whatever the primary cause of her illness, this patient, he felt, was "now riddled with a virulent Staphylococcus aureus, which is so resistant to the antibiotics that their use would be of questionable value."

Although up to this time the patient had appeared surprisingly well, she suddenly became very weak and exhausted, displaying marked addisonoid symptoms. She became dehydrated and she was unable to swallow food because of the pain of the pharyngeal lesions; it was no longer possible to find open veins for intravenous administration of fluid. Tube feedings were started, 2,000 cc. of a high caloric mixture made up to 3,000 cc. with water being given daily. Dr. Kendall kindly supplied us with a quantity of his extract of the adrenal cortex, 100 cc. being given intramuscularly. The patient seemed to show a sudden marked improvement after this injection but the next day her temperature rose to 106° F. and remained there and she died in the afternoon, apparently of exhaustion.

The Section on Pathologic Anatomy made detailed examinations of the tissues of this patient. Five months later they reported that the case was still a puzzle to them. They found numerous abscesses of the skin and mucous membranes from which they could culture only Staphylococcus aureus. The internal organs showed absolutely nothing in the way of any specific change either as a basis for the involvement of the skin and mucous membranes or as a secondary manifestation of it.

The most striking things about this patient's illness appeared to be a rather startling appearance of well-being in the face of a serious disease, the lack of any marked response of the hemopoietic system to the infection, the lack of the usual leukocytic barrier to the invasion of tissues by micro-organisms and the daily high fever with apparent lack of the usual co-ordination between the febrile and leukocytic reaction to infection.

The absence of subjective illness, as well as the lack of response of the specialized defense tissue, both apparently indicate a disorder of function of the normal defense mechanism of the body.

CASE 2.—This patient, a man aged 45 years, was referred to the Mayo Clinic because of nasal and orbital symptoms. The referring physician stated that the patient, who had reported nasal sinusitis for "years" had first come to him two and one-half years previously because of swollen lymph nodes in the neck and axillae, following a series of slight colds. Examination then revealed palpable lymph nodes in the cervical, axillary and inguinal regions and a palpable spleen. A roentgenogram of the thorax was reported to reveal normal cardiac and lung field shadows. The mediastinal lymph nodes were not enlarged and there were no findings to suggest a mediastinal lymphadenopathy.

Examination of the blood taken at that time had showed 80% hemoglobin, 4,850,000 erythrocytes and 68,600 leukocytes per cmm., of which 90% were lymphocytes, 9% neutrophils and 1% eosinophils. The results of a complement fixation test for syphilis were negative. In the next two years repeated blood counts were taken. The patient was said to have received "some" roentgen treatment. In spite of this there was little change in the blood picture or roentgenographic findings. A diagnosis of "pseudoleukemia" appears to have been made. A year and four months before coming to the Mayo Clinic the patient had noticed swelling around both eyes and a profuse yellow purulent discharge from both sides of the nose, but he had not experienced any pain. Since its first appearance the swelling around the eyes had appeared and disappeared, affecting sometimes one eye and sometimes the other. The patient reported that just before he came to the clinic a roentgenogram of the head was reported to reveal destruction of the ethmoid plate with extension of infection from the ethmoidal cells into both orbits. The physician who referred the patient to the clinic made a diagnosis of "granulomatous rhinitis and sinusitis, with progressive osteomyelitis of the bones of the face."

On examination at the clinic the patient did not appear to be acutely ill. Examination of the nose showed both nasal chambers filled with thick crusts and on removal of these crusts the mucosa was seen to be covered with a thick, tenacious, yellow, purulent exudate. The mucosa had a "peculiar" appearance, markedly thickened and "hyperplastic." On examination of the eyes the right lid was found to be reddened and greatly swollen. There was a fistula draining pus on the medial aspect of the right upper lid. There was a slight chemosis of the conjunctiva on the right and a slight proptosis but no limitation of motion. It was noted that blowing of the nose forced air through a fistula on the medial aspect of the left upper lid but not through the similar fistula on the right.

General physical examination revealed little except a "good number" of palpable lymph nodes in both axillae and a few in both inguinal regions. The spleen was palpable but the liver was not palpable. Examination of the blood showed a concentration of hemoglobin of 11.9 gm. per 100 cc. with an erythrocyte count of 4,840,000 per cmm. There were 18,600 leukocytes present per cmm. Differential count showed 17.7% lymphocytes, 6% monocytes, 76% neutrophils and 1% eosinophils. After examining blood smears the hematologist reported that a leukocytosis with lymphocytosis was present. There were no immature forms seen and it was felt that the blood picture resembled that char-

acteristic of a toxic process. A sternal puncture was done and the hematologist reported that although a leukocytosis with about 60% lymphocytes was present, he was unable to find any immature cells to substantiate a diagnosis of chronic lymphatic leukemia. Another sternal aspiration was done in the usual manner and a satisfactory specimen was obtained. There were many units and they varied greatly in size. Examination of the unconcentrated and concentrated smears showed an unusually large number of mature lymphocytes with bluish cytoplasm and a rather heavy blocked chromatin nucleus. Other bone marrow elements did not seem to be particularly disturbed and on the unit touch preparations it was seen that these lymphocytes occurred in masses and spread out in chains. There were essentially no mitotic figures present and the lymphocytes looked mature. The fixed preparation was very good and showed the bone marrow to be largely replaced by lymph follicles. Again there were no mitotic figures present and the lymphocytes looked mature. The hematologist stated that "this should be a chronic lymphatic leukemia although we would be unable to differentiate it from a lymphosarcoma."

Roentgenograms of the sinuses revealed cloudiness throughout. The result of a flocculation test for syphilis was reported to be negative. Cultures from the nose were reported to reveal a streptococcus (hemolytic) and a micrococcus. A culture from the orbital abscess planted on hormone blood agar (P&S) and dextrose agar did reveal fungi, but a culture on ordinary mediums showed many colonies of hemolytic streptococci. A culture taken from the right sphenoid was reported to reveal Staphylococcus aureus with a sensitivity to penicillin between 100 units and 10 units per cc. On another culture from the nose many colonies of gram-negative rods which were felt to be pseudomonas were found. Sputa examined were negative for sulfur bodies and acid-fast bacilli. The sedimentation rate by the Westergren method was 28 mm. per hour. On the basis of these examinations it was felt that the condition present was "compatible with a diagnosis of lymphosarcoma or leukemia." Roentgen therapy was advised and was given over the orbits, sinuses and splenic region. The patient was dismissed and told to return in a month. After dismissal he was able to return to his work as a bank clerk, but a week before his return he caught a slight cold with marked increase in the swelling and induration about the eyes. Except for this increased swelling, the patient's condition was about the same as on dismissal. Further roentgen therapy was given with an apparent marked improvement in the condition of the induration about the eyes. During the patient's stay in the hospital on these two occasions he received 160,000 Oxford units of penicillin every 24 hours.

This patient returned again in two months because dermatitis of his upper lip and right ear had developed. All penicillin therapy was stopped and the dermatitis cleared up in a month under wet dressings with 1:16,000 potassium permanganate solution. During the interval that the patient had dermatitis his nose and eye condition seemed to improve markedly.

He returned again in about two months with a marked flare-up in his nasal and orbital symptoms following a slight "cold." At this time his blood count showed 6,700 leukocytes per cmm. and a blood smear was reported to show mild lymphocytosis with some cells a little immature. The general medical consultant felt that there was insufficient adenopathy or blood changes to warrant further roentgen therapy.

At this time the ophthalmologist expressed the opinion that the sinus infection was maintaining the disease in the eyes and since the medical men were

now inclined to doubt the diagnosis of leukemia, it was decided to try the effect of surgical treatment of the sinuses.

Bilateral naso-antral windows were made and both sides were found to contain a large quantity of foul pus with a tremendously thickened and degenerated mucosa which was curetted out. The middle turbinates on both sides were infracted toward the midline and the ethmoidal labyrinths were entered through the bulla ethmoidalis on both sides. The anterior and posterior ethmoidal cells on both sides were very seriously diseased and on opening into the sphenoidal sinuses both were found to be similarly involved. Very large openings were made from the nose into both frontal sinuses. Both were found filled with foul pus and diseased membrane. After removal of the diseased tissue on the right side an area of dura measuring about 2-3 cm. and covered with infected granulation tissue was revealed. The dura in this area could be seen to pulsate. The middle turbinates on both sides were preserved in their entirety.

After the operation the patient seemed to make a spectacular recovery. The orbital lesions cleared up, the nasal discharge stopped and he seemed to have regained excellent health. Five months later, however, he contracted a "cold in the head." Two weeks later he was brought into the hospital in an apparently serious condition. Perforations had developed above the inner canthus of both eyes, there was a return of the purulent nasal discharge, the patient had lost much weight and he was severely short of breath.

The consultant in general medicine felt that the condition resembled a chronic infection rather than a leukemia. Blood counts taken at the time showed 22,000 leukocytes per cmm. with 21% lymphocytes and 76% neutrophils. Blood smears were reported to show leukocytosis with toxic polymorphonuclear leukocytes. There were some very abnormal, rather immature lymphocytes. It was felt that the blood smear was not diagnostic. The hematologist expressed the opinion that the condition was definitely not chronic lymphatic leukemia but probably represented some kind of lymphoma which might be on an infectious basis. A roentgenogram of the thorax showed fluid in the left pleural space with displacement of the heart toward the right. The thoracic consultant felt that if he had nothing but the roentgenogram of the thorax and findings to go on he would strongly favor a diagnosis of tuberculosis, but he was not sure if this would fit in with other features of the situation. Thoracentesis was done and 600 cc. of clear dark brown fluid was removed without difficulty. The fluid was found to have a specific gravity of 1.018 and contained 1,900 cells per cmm.; there were 285 mg. of fat per 100 cc. and 3.3 gm. of protein. The pleural fluid was found negative for bacteria and negative for acid-fast bacilli.

The patient was given 1,000,000 Oxford units of penicillin per 24 hours and appeared to be making favorable progress when at 1:30 p.m. of the sixth day after admission he suddenly became orthopneic and cyanotic and appeared to be in a critical condition. It was felt that a pneumothorax had developed on the left. Three chest taps were done, withdrawing more than 2,000 cc. of air and about 200 cc. of cloudy yellow fluid. This did not improve the patient's condition and he died during the night.

Pathologic examination of the body of the patient failed to resolve the dilemma as to the type of condition. After exhaustive examination of microscopic sections the pathologists reported this case to represent a "lymphoma." They could not classify it further.

The striking feature of this case seemed to be the patient's lack of resistence to mild infections of the upper part of the respiratory tract. Each infection would cause a tremendous inflammatory reaction in the midline tissues of the face, suggesting bacterial hyperimmunity in the area with an "Arthus" type of reaction to indifferent intercurrent infections. During the entire course of the illness the patient's temperature never rose to more than 100° F. He reacted to mild stress very much like an adrenalectomized animal.

CASE 3.—A man, aged 21 years, was admitted to the hospital for emergency treatment. Since he was from Mexico, his examination had to be conducted through an interpreter. He stated that seven months before his admission congestion of the right side of the nose had developed. Two weeks later a "canalization" into the right maxillary sinus had been done. Pain and tenderness of the right malar region had developed almost immediately with hyperesthesia of the upper teeth on the right. A thick sanguinopurulent exudate began to run from the right side of his nose almost immediately and continued without interruption until his admission. He began to have a fever. A month before his admission the process extended to his right ear and subsequently the ear discharged continuously. A short time before his admission inflammation and induration extended into the upper part of the right side of the neck.

Examination was done with some difficulty because of a very low pain threshold. On examination of the ears, nose and throat, after shrinkage, both nasal chambers were found filled with a granulomatous mass which bled easily. Specimens were taken, biopsy of which was reported to show very inflammatory tissue with numerous polymorphonuclear neutrophils and lymphocytes, also eosinophils and plasma cells. The right upper gingiva was swollen and tender. The right ear was filled with a thick sanguinopurulent exudate which on removal revealed a perforation in the postero-inferior quadrant of the eardrum.

The result of ophthalmologic examination, including examination of the fundi, was negative.

On general physical examination the patient was reported to appear obviously ill with pains "everywhere" in the hands, feet, abdomen, thorax and neck. Nothing was found on examination except some enlarged nodes in the axillae and groins. The patient's temperature was 102° F. Roentgenograms of the mastoids were reported to be negative, but those of the sinuses were reported to show thickened membrane in the right antrum, both ethmoid cells and frontal sinuses. A roentgenogram of the thorax was reported to be negative.

Examination of the urine revealed the presence of erythrocytes, grade 2 to 3 (on the basis of 1 to 4, in which 1 indicates the least and 4 the greatest deviation from the normal). Examination of the blood showed 14.8 mg. of hemoglobin per 100 cc. of blood. There were 17,000 leukocytes per cmm. and differential count showed 18% lymphocytes, 4% monocytes, 76% neutrophils and 2% eosinophils. A blood smear showed toxic polymorphonuclear leukocytes containing Döhle bodies. There were considerable left shift, mild hypochromasia and increased regeneration. The results of repeated examinations of sputum were reported to be negative for Mycobacterium tuberculosis. A thick blood smear was negative for plasmodia. Agglutination reactions were negative for Brucella,

typhoid and paratyphoid organisms. The result of a coccidioidin skin test, first strength, was reported to be positive, 2+. Repetition of this test with the second strength gave the same result. Cultures of the sputum on dextrose agar and hormone blood agar were negative for fungi. Cultures of pus from the ears and nose done on brain broth blood agar were reported to reveal the presence of hemolytic streptococci. Blood cultures were negative.

Owing to the fact that the patient's illness might be due to general invasion from the antrum, it was advised that the nose and antrum should be explored.

At operation the nasal chambers were found to be completely filled with granulation tissue. This appeared to have originated from the septum, which had been completely destroyed by the disease. The right antrum was found to be normal but both ethmoidal labyrinths contained granulation tissue and pus. Histologic examination of the tissue removed at operation showed a very inflammatory tissue with numerous polymorphonuclear neutrophils and lymphocytes, also eosinophils and plasma cells. Tissue cultures from the material secured from the nose and sinuses were positive for hemolytic streptococci but were negative for other bacteria or fungi.

The patient's condition failed to improve after the operation. One gram of emetine hydrochloride and 300,000 units of penicillin were administered every 24 hours and he was given a high-vitamin, high-caloric diet.

On the third day following operation the patient began to cough and complained of a pain in the thorax. A roentgenogram of the thorax showed pneumonitis at the right cardiopleural angle, and on repetition a week later the roentgenogram showed some pulmonary congestion in both lower lobes. The patient began to complain of increasingly severe epigastric pain. A liver function test revealed dye retention, grade 3. The direct van den Bergh test for bilirubin revealed 1.2 mg. per 100 cc. of serum and the indirect test, 0.5 mg. per 100 cc. Owing to continuing hematuria an excretory urogram was done and was found to be negative. The source of the hematuria could not be determined by the urologist in the absence of cystoscopy, which was felt to be contra-indicated.

Sternal puncture and aspiration were done. Some small units were reported to be present, some floating and some sinking in the fixing solution. Examination of all the preparations showed a moderate cellularity, primarily of the neutrophilic line with a left shift. A majority of the cells, particularly on the touch preparations, were in the premyelocytic stage. On the concentrated smear a large number of mature polymorphonuclear leukocytes were present, and at the fringe there were a number of both phagocytic reticulo-endothelial cells and monocytoid reticulo-endothelial cells. The phagocytic cells contained pigment debris and occasionally some dark-staining material which it was felt might be nuclear debris. No organisms suggesting fungi or bacteria could be found in any of these cells. It was felt that the bone marrow was "not diagnostic" although of the type usually seen in an infectious process. The patient continued to have a high temperature, to have erythrocytes in the urine and appeared very toxemic. There suddenly developed an eruption of a purpuric and vesicular type on the soft palate, also tending to occur in patches chiefly over the sternum, buttocks and lower back, elbows and forearms. On the soft palate were small (1-2 mm.) inflamed yellowish ulcers with red areolae. They were diffusely scattered over the entire surface of the soft palate. The lesions on the skin were elevated, infiltrated skin-colored plaques

associated with some firm acuminate papules. There were also a few hemorrhagic blebs and firm pustules with umbilicated centers. Examination of the blood at this time showed 6.0 gm. of hemoglobin per 100 cc. of blood and 2,450,000 erythrocytes and 10,800 leukocytes per cmm. of blood. Differential count showed 25% lymphocytes and 74% polymorphonuclear leukocytes.

The dermatologic consultant felt that these cutaneous lesions might be anaphylactic. Blood transfusions were started. A gallop rhythm with definite electrocardiographic changes suddenly developed. The following comment was then made by the consultant in internal medicine, "The patient has added another to the number of systems involved. The multiplicity and particularly the organs involved fit in well with the diagnosis of periarteritis nodosa. The low percentage of neutrophils in the differential count and the lack of response to penicillin are against an abscess of cryptic nature unless it is a granuloma." Biopsies were made of an axillary lymph node, a portion of the pectoralis major muscle, a small artery and a small vein. The pathologic report was: "Inflammatory lymph node. Normal muscle and artery. The vein shows slight perivascular infiltration about capillaries in its wall." Cultures of the tissues removed were negative for bacteria and fungi. Pulmonary edema developed and the patient died.

Necropsy revealed extensive granulomatous lesions in the trachea and bronchi. Small, yellowish nodules were found scattered throughout both lungs, especially in the lower lobes. Microscopic examination disclosed a large number of necrotizing lesions of the pulmonary arterioles and parenchyma as well as extensive granulomatous inflammation of the bronchi. Lesions of periarteritis nodosa were also found in the kidneys, liver and spleen.

The onset of the disease in this patient was more sudden and the course was less prolonged than in the others. The patient showed more evidence of illness with the disorder than the usual patient with lethal granuloma. This illness seems to be the reflection of active resistance. The leukocyte count, however, never rose to more than 17,000 per cmm. of blood and the percentage relationship between lymphocytes and polymorphonuclear leukocytes was never disturbed. It might seem that when there is a partial leukocytic response the larger vessels appear to be more involved with periarteritis nodosa, and when the leukocytic response is less marked the capillaries are involved in an "Arthus" lesion.

SUMMARY

Data on three cases of lethal granulomatous ulceration of the midline tissues of the face are presented. It is suggested that granuloma is the stereotyped defense mechanism by which the body resists invasion by micro-organisms which are feeble toxin producers. This same defense mechanism is utilized by the body when nontoxic protein material is injected.

Tissue immunity as outlined recently by Kahn[15] is the immune mechanism involved. Dysfunction of this immune mechanism may occur as the result of hyperimmunity in certain areas with the development of the Arthus phenomenon or periarteritis nodosa or both. Evidence suggests that both these lesions are produced by the same physiologic mechanism, affecting in one instance the capillaries, in the other the smaller arteries and arterioles.

According to Selye[31] periarteritis nodosa may be produced by excess of the "salt-active" corticoids of the adrenal glands. He suggested the hypothesis of relative adrenal cortical dysfunction with excess production of the "salt-active" and relative suppression of the "sugar-active" corticoids. He has found that excess sodium ion and an increased pH favor the development of periarteritis nodosa under experimental conditions whereas elimination of sodium ion together with the giving of acidifying drugs will tend to prevent its development. Whether the interpretation of the experimental results obtained by Selye can be applied in clinical medicine must await further investigation. The availability of the hormones of the adrenal cortex will make possible new approaches to the study of granulomas and may answer some questions which have long been apparent.

MAYO CLINIC.

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DISCUSSION OF NEW AND WILLIAMS PAPERS

FREDERICK T. HILL, M.D.: Speaking of Dr. New's very interesting paper, I am wondering if the matter of recurrence and necessity for reoperation would depend, at least to a certain extent, upon the question of whether the granuloma was completely sessile or at all pedunculated. In a case of mine of bilatral granulomata following intratracheal anesthesia reoperation was necessary on the side which was sessile. I am wondering whether those of indeterminate origin might tend to be sessile, rather than pedunculated.

PAUL H. HOLINGER, M.D.: Mr. Chairman, Dr. New has certainly presented a very complete discussion of this subject and has made us cognisant of the frequency of contact ulcers of the larynx. We differ with him in one point and find that the soft granuloma seems to respond more readily to therapy than does the longer duration, hard, granulomatous mass. Further, we have found no association between the side of the referred pain and the side of the granuloma. Occasionally the granuloma produces pain, while in most cases pain is associated with the actual ulcer on the opposite cord.

The significance of voice training I think is well understood, and has been stressed by the speech correction therapist working with us. The pathology seems to change less rapidly than one would expect from the improvement in symptomatology which follows the beginning of proper voice training. We agree with Dr. New that the surgical excision should be followed by voice training.

I would like to add three cases to the group of post-anesthesia granuloma patients that Dr. New presented: one a unilateral granuloma and two bilateral.

(Slide) This slide is a photograph of a unilateral post-anesthesia granuloma taken through the direct laryngoscope. The granuloma is on the patient's left vocal cord. The characteristic appearance of the soft granuloma on the tip of the vocal process is distinctly different from the exudate covered granulations of true contact ulcers.

(Slide) This shows a bilateral, soft lesion. A considerable space separates the posterior commissure and the site from which the lesions apparently have their origin; in other words, they appear to originate closer to the tip of the vocal process than is the case of true contact ulcer which in our experience involves the entire phonating edge of the vocal process of the arytenoid, or more particularly its posterior portion.

NORTON CANFIELD, M.D.: I had an opportunity to see three cases following the use of intratracheal tubes during anesthesia.

In regard to Dr. Williams' paper, I have seen two cases of the kind he described, the first one in 1936 and the last one in 1944, in an Army hospital. This patient's trouble started with a slight injury to his upper lip which began to swell the same day. This continued as a very slight swelling for about three weeks and was not thought to be very severe or of any great consequence. However, the same destructive process that Dr. Williams has described gradually ensued and in spite of extensive chemo-and antibiotic therapy went on to a fatal termination.

FLETCHER D. WOODWARD, M.D.: I would like to report a case of unilateral, contact ulcer granuloma of indeterminate origin with a broad sessile base, situated on the posterior end of the cord and arytenoid process. This mass has been removed endoscopically and the base cauterized three times and was approximately the same size each time, one centimeter in diameter. At the last operation I felt convinced that this process went deeper than I had previously supposed, that in addition to the perichondritis of the arytenoid process there was actually a chondritis of the cartilage. I feel that if this tumor mass reoccurs, an arytenoidectomy will be necessary.

EDWARD D. KING, M.D.: I would like to ask Dr. Williams whether he has had any experience with the therapeutic methods he has described. I saw a lethal granuloma in a Filipino during the past winter.

GORDON B. NEW, M.D. (closing): Regarding Dr. Hill's question about the sessile, pedunculated tumors, I think most of those in the indeterminate group in my experience have been sessile. I am glad Dr. Holinger showed the pictures because I wanted you to compare those of an artist and a master with the ones of amateurs using his camera. I want to congratulate him on these beautiful pictures.

Regarding the point he brought out that the soft granulomas get well easier than the others, I wonder if it is not due to the fact that all the cases he presented were postanesthetic cases which in our experience all get well whether they are fibrosed or of the soft inflammatory type.

Regarding Dr. Woodward's question, we have had to remove some of the vocal process of the arytenoid as a sequestrum in some of the cases of indeterminate origin.

HENRY L. WILLIAMS, M.D. (closing): We have not had the opportunity of trying therapy with compound "E" of Kendall on lethal granuloma but this substance has been given for some of the related conditions, particularly lupus erythematosus and rheumatic fever, with favorable clinical results. I feel, therefore, that I am not altogether out on a limb in suggesting this treatment for the granulomatous lesion.

AN INTERNIST LOOKS AT SPECIALISM

Joseph C. Doane, M.D. (By Invitation)

Philadelphia, Pa.

Dr. Norbert Weiner, Professor of Mathematics at Massachusetts Institute of Technology recently wrote that since Leibwiz there has been no man who has had a full command of the intellectual activity of his day. Since then science has been the business of specialists whose fields grow ever narrower as human knowledge increases. This can be truthfully said of the field of medicine, both individual and institutional. Perhaps Osler in our day came as near being the modern Leibwiz as any.

Three hundred years ago hospitals were but places of relative warmth, of meager food, and of safety from marauding savages. A hundred years later little more was known as to the recognition and treatment of disease, and hospitals were staffed with men little learned in the science of medicine, and certainly specialists in nothing except as in the case of Benjamin Rush, in egotism and self assuredness. When by the use of Von Loewenhoch's lenses a new world peopled with hitherto unsuspected micro-organisms was discovered, the specialties of bacteriology and later immunology were born—the doctrine of asepsis gave greater scope to the surgeon's scalpel, and the discovery of the x-ray and electrocardiograph created new special fields in which physicians might labor. But to the concern of many without and within the profession specialties have too often developed into autonomous kingdoms of activity. Let us turn to the vocabulary of the mathematitian for a moment to illustrate the mechanism of this development.

Cybernetics is a term fresh from the mint of the great minds of Weiner and Rosenbluth who for many years have been studying the relationship of all aggregates of molecules to all other such masses. This term by its Greek derivation means helmsman, moderator, or regulator. It implies that in all the world there are no aggregates of molecules that are not related in some degree to each other. If I crook the index finger of my hand it affects the tides on the most distant star. Perhaps this statement of the scientist is not too fan-

tastic. Its language is as unknown to many of us as would be the Greek from which it gets its name, to the new born. For example, I find myself in a state of entropy which, cybernetically speaking, means a deterioration of organization to a state of complete random as I approach a subject of such magnitude as that assigned to me. And yet perhaps I may apply the term cybernetics of medical practice to this talk, using some of the terms of this new conception to illustrate my theme.

Feed backs is a term used by engineers. It refers to the system of controls which are constantly active in mechanical or human movements, and by which at some point there is a constant awareness and regulation of activity elsewhere. In mechanics the governor controls the steam supply and hence the speed of an engine. In medicine, DuBois believes that an automatic regulatory mechanism or feed back exists which prevents excessive body temperature.

As knowledge of the basic sciences grew and as it was seen that no one man's mind could excel in all, specialties began to emerge. Medicine could not have escaped from its dark ages otherwise. But has the system of feed backs been so developed that the womb of general medicine from which specialism was born, is in any any very certain way related to these explorers in distant fields and visa versa. Has there developed such a lack of coordination between and among the recognized specialties that a real atoxia of effort has resulted. Just as the finger of the cerebrospinal luetic has difficulty finding the tip of his nose, so it is often a long way from the head mirror of the laryngologist to the electrocardiographic strips of the cardiologist, although these may be very closely related in the pathology which each discovers or suspects. Here the feed back controls are often lost and each specialty, living more or less in an atmosphere of its own, loses its intellectual and practical contacts with others. Thus it becomes a matter of using lenses of very great magnifying power but which are capable of viewing but a very small segment of human anatomy or behavior. We must always remember that the infected finger viewed by the surgeon, is a part of a hand, arm and body of the diabetic or the cardiac.

Ever and anon, a new yet old meteor of specialism flashes across the medical sky, and at length pales and vanishes. The newly acclaimed specialty of psychosomatic medicine is as old as medicine

itself, and none who have successfully treated the sick since the days of Hippocrates have done so without, consciously or unconsciously practising it. Geriatrics is a newcomer in the field of specialism and its only claim for recognition exists in the fact that the physician who knew how did not give the aged proper consideration. One is reminded of the alarm of the dear old lady who on being told that her grandson was now a naval surgeon remarked, My, my, how specialized abdominal surgery has become.

A little over three decades ago a notice in the village paper that the doctor had departed for a medical center to study some branch of medicine made him a specialist on his return. It can not be denied that all of us want to be professors and none will long sit contentedly on the benches. I now direct attention to some more concrete considerations of this subject.

1. Of what stuff is the specialist made.

2. How are specialists made.

3. What are the results of this process as expressed in terms of human behavior and benefit.

For three decades I have been endeavoring to teach young men and women who in earlier days could be induced to study medicine and who in the past two decades could cajole or coerce medical schools to accept them. Many made fine American physicians and kept inviolate their Hippocratic oath. Some, however, should have aspired to be blacksmiths, and I mean no discourtesy to Longfellow's hero. I am convinced that the future of American medicine lies in the hands of the Deans and Admitting Committees, of medical colleges. Secondly, I am sure that no college or curriculum—no specialty hospital training or examining board can create ethics, intellectual honesty, or morality where their germs were not present at birth. It would be as easy to fashion a whistle from a porcine appendage or a purse from the ear of a female porker as to make a good doctor—an honest and trustworthy specialist from unworthy and immoral human material, no matter how intellectually scintillating. There is a specialism of the heart as well as of the head of our medical forefathers 'twas said by Kipling:

Precious little when all 'tis said
Precious little our fathers knew
Most of their remedies cured you dead
Most of their teachings were quite untrue
But Iowa from the heavens or up from
the mold
Send us the heart of our fathers of old.

Perhaps the process of cramming which is medical eduaction of today should be so reorganized that basic sciences are better taught and some of the ultra modern theories and conjectures are left for the post graduate days. A commendable trend is the contact of patients by students early in their course. And how do specialists come into being. Prior to 1916 they defied the Biblical injunction to let others praise them and not their own voice. They, like Topsy, were not born, they just grew. Even today there rises up here and there a would be Moses crying in the wilderness that he has a cure for arthritis, asthma, or cancer, and a gullible public sell their worldly possessions to seek such false meccas of healing. To bring some order out of this chaos the Advisory Board of Medical Specialties was organized in 1933, with the avowed purpose of coordinating education and certification of specialists in the United States and Canada. There are now sixteen specialty Boards in existence—the first being that of Ophthalmology, and the second of Laryngology organized in 1916 and 1924 respectively. All have carefully worded statements of purpose and organization. All detail qualifications for candidates. All require membership in the American Medical Association, and that the aspirant be honest and ethical. All indicate that certificates granted may be revoked for cause. But two, to my knowledge, these being anesthesiology and Physical Medicine, threaten revocation if the Diplomate fails to practice his specialty 100% of his time. None set up any machinery for future confirmation of the eligibility of the Diplomate. Surely, this is a marriage not only for time but also for eternity. This policy does not prevent the writer from practising obstetrics or laryngology if he could catch some one off guard, and the Board of Internal Medicine would probably not overtake him for many years. By the same token many layers of moss could accumulate on the medical journals of a Diplomate and his shadow never darken the door sill of a medical library or meeting, and yet he remains one of the elect.

A comparison of examination fees is intriguing. To take the Board of Urology is most expensive, $150, but one may take the American Board of Pathology for $35. I suppose this variance reflects the difference between the $1000 for opening the urethral sluice way and the $10 for performing a Wassermann. Even then I think the Urologist is under charged. Most Boards set a definite fee of from $75 to $100. Would-be specialists in Pediatrics and Ophthalmology must pay $125 for examination. Many of us looking over the specialty menu and not being wise enough to become pathologists, chose the next in order of expense and become Diplomates of the Board of Internal Medicine for $40 plus $10 for our shingle. We also carefully estimated the risk and later expense of failure—for if one fails in Ophthalmology or Pediatrics a whole re-examination costs $75 while in Internal Medicine one may be obtuse and ill informed, and the oral re-examination costs but $20. There are some advantages you see in being an internist even without the acknowledged advantage of prostates, tonsils, and vermiform appendices. But not all physicians can and many should not aspire to become Board Diplomates. Indeed, there is not a little tarrying at the wailing wall by those who bemoan specialism as a Frankenstein threatening the welfare even the life, of the less geographically and economically fortunate. Observe what happened to the carrier pigeon, say they, and consider the likelihood of such a fate befalling the general practitioner. But let us remind you the latter is a hardy perennial who can well withstand the frosts of superiority which descend on him because of the rise in specialism. Of the 165,000 practising physicians in the United States, about 30,000 or one out of 5½ are Diplomates of some specialty board. Many of the remaining 4½ of this number are practising more or less pure specialism, and are not holders of certificates because they early did not choose to qualify and now do not feel inclined to try. Many are in administrative and governmental posts and are not engaged in the practise of medicine at all. It is difficult to secure accurate figures on this matter, but it is more than a conjecture that approximately 20% of all practising physicians in the United States have qualified as specialists in some field of medicine. Now the general practitioner presses for some type of recognition, and as a result the American Academy of General Practise has come into being. There are many who believe that this is not the solution to the problem of encouraging young physicians to enter general practise believing that no good follows the organization of what some have

considered a pressure group. Nor is it certain that it is fair to those especially equipped, or what is more important, to patients, to build into the hospital staff organization, a department of general practise. This would be weakening the fine stimulus to study created by specialty boards and would in fact give to such staff men more privileges than to those whose institutional rating limits them to one type of work. There are those who deprecate the tendency clearly indicated in current hospital practise to encourage or require that visiting physicians and surgeons qualify as specialists to secure or even hold their posts. Sometimes this qualification extends to associates or even to assistant physicians. One who has observed the majority of his staff prepare for and finally pass the examinations of the Board of Internal Medicine, cannot but remark their changed approach to the study of a patient because of greater interest in and knowledge of the modern and scientific aspects of disease. As to the 20% on whose office walls hang a specialty certificate one wonders at the rapidity of increase, and as to when the saturation point will be reached. The 2nd edition of the Directory of Medical Specialists contained 18,000 names. In 1946 there 23,000 and in 1948 29,000. No doubt there exist several explanations for this increase of 66% in six years. Moreover, many factors must influence the physicians in his choice of specialty. In Philadelphia, Diplomates of the various Boards number as follows:

Internal Medicine	195	
Laryngology	131	
Obstetrics and Gyn.	118	
General Surgery	116	1044 out of 3500
Psychiatry and Neur.	112	30% or 3 out of 10
Radiology	87	1 doctor for 650
Pediatrics	79	
Ophthalmology	72	1 specialist 2230
Pathology	49	
Urology	40	
Dermatology	33	

At the bottom of the list are found Physical Medicine—3, and Anesthesiology—9. Governmental subsidies to veterans, the demand by many hospitals that staff physicians become Diplomates, the payment by the Veterans Administration of 15 to 25% more salary than

to others no doubt all served to increase this trend toward specialty training.

I now would direct your attention to some dangers in this modern development as I see them. The fundamental experience and training of the physician may be considered as the base of a pyramid, the sides of which as interest and information becomes more localized, ever become more acuminate. Some times the specialist finds himself balanced on such a sharp and brittle pinnacle of localization and so far removed from the stable base which is the patient as a whole, that he is likely to topple from his own weight. But I would not deprecate the accumulation of knowledge about matters that in our time will never be brought to a patient's bed. All hail to him who knows how many hairs on back of a civet cat or how often there are peristoltic movements in the intestines of the musca domestica. Such accumulations of information increase the sum total of human knowledge and train the minds of men to know man and God better. Some develop diagnostic presbyopia, others become professionally haughty. There is a difference between thinking that you know, and knowing what you think. Others are so scientifically provincial that they conclude that every presenting symptom can or should relate to his specialty. A young surgeon examines a man with a right lower quadrant pain. He diagnoses appendiceal infection, and removes a normal appendix. But he failed to evaluate the presence of a mitral stenosis with fibrillation and red blood cells in the urine. A few days later autopsy showed massively infarcted kidneys. A medical opinion here might have helped. The prayer of the iconoclast "God deliver me from too many specialists with narrow gauge one track minds" has some justification. None of us have at our command so potent pills and procedures that more than a few conditions will yield to their use.

At a dinner celebrating the 50th year of practise of a distinguished Oto-laryngologist, the toastmaster read this suppositious letter—'Dear doctor, my husband has halitosis, is a Democrat, beats me when angry, chews tobacco and has dermato phytosis. Do you think you could cure him by taking his tonsils out?' An old neurologic friend of mine bemoaned this toothless, gutless age which resulted when speculation ran wild as to the role of focal infection in the cause of systemic disease. The mania for removing organs sometimes follows this specialty provincialism of which I spoke—

and it can in the economically greedy or the shallow thinker, only be cured by the use of padlock and chain on any tissue which is not vital to life.

I hasten to disavow any intention of belittling the splendid achievements of the distinguished men in the field of laryngology, neuro-vascular surgery, and in many other fields. But, I am urging maintaining a broad base of extra specialty information which will cause the surgeon to be known not because he carries no stethoscope, and the internist to know of vagotomy and the newest approach to the optic thalmus. Perhaps all specialty examinations should be largely general in complexion on the first day, and passing these, the applicant could then prove the presence of adequate specialty knowledge. Perhaps there should be developed a system of exchange examiners. Would it be too revolutionary for the Board of Internal Medicine to include a question on laryngology, orthopedics, or pediatrics in its written examination? Would it not explore the applicant's breadth of knowledge for an internist to prepare a question on heart disease or nephritis or calcium deficiency for the examination of the would-be surgeon, ophthalmologist, neurologist, or obstetrician? Even when all specialized services are available on a hospital staff, the surgical ward is often a day's journey from the medical wards professionally speaking. We have in many locations yet to find a method of quickly focusing all types specialty information on the patient's bed—even though many opinions are quickly secured (and this is rarely so, for you know Dr. Jones does not visit the hospital on Wednesday), the proper interpretation and application of these often illegible comments is long delayed. The family doctor often renders a great service in being the one to judge when a consultant is to be called. Many of our best hospitals have much to learn relative to good group medicine. 'Twould do all of us good who are practising on the periphery of the medical wheel to return now and then to the hub from whence we sprang and relearn that our strength originated there and is still dependent on it for unity.

I apologize for taking so much of your valuable time. I have solved no problems. I have, like Omar Kyam, "frequented both doctor and saint and heard argument about it, but ere came out by the same door in which I went." But I have endeavored to follow the admonition of the Apostle Paul in regard to the subject of spe-

cialism, "If there is anything virtuous, lovely, or of good report or praiseworthy, we seek after these things."

Finally, I can conclude this paper in no more suitable way than to quote the closing words from an address of your much revered Dr. Harris P. Mosher: "The strength of specialism is specialism. Paradoxically, its weakness also is specialism."

269 South 19th Street.

DISCUSSION

Burt R. Shurly, M.D.: It is a great delight to hear this paper bring us into a wider field of thought and endeavor. As we go down these corridors of time, and after 50 years in the practice of medicine and with a nervous system which still allows us to think gently and quietly at times, it seems to me that we are today facing one of the greatest problems in medicine, and that is to be doctors first and specialist later on, yet doctors all the time.

The joy of the practice of medicine is indeed great when we realize that we must know the patient, the individual, better and better. It seems to me that the need for a greater study of the individual, a greater study of what that individual stands for, what he is, what he is doing, and not in his pocketbook or some other peculiarity of that individual. That is timely. I believe as we overdo specialism it grows narrower and narrower in many of its fields. It is time to awake again to the fact that we are the student of the individual and his doctor.

Perry G. Goldsmith, M.D.: I appreciate very much Dr. Doane's remarks and I know of nothing that is more necessary in our Society than having someone give his opinion of our short-comings. Realizing my own short-comings better, probably, than many of you do I naturally hesitate in discussing them but as the question is a sort of hobby with me I hope you may accept them, not only as evidence of my grace of humility but as an earnest wish to advance otolaryngology.

I have been one of the Examiners on the Board for many years certifying men as safe and fit to be called Specialists in Otolaryngology. I only occasionally find one who has a sound comprehensive knowledge of internal medicine. In fact, I asked one man some questions about the larynx, especially regarding hoarseness, and he replied that in his clinic he only treated the nose. He did not seem to be much upset by my asking him "Which nostril was his field."

I think most of the errors Specialists of all sorts make are due to neglect in securing a good history. The diagnosis, or at any rate, reasonably probable opinion will be found in the history if it is a good history. A history consisting of a few lines written on the back of a card the size of a post card, is probably of no use at all. The time taken to write a good history containing the medical and personal record of the patient and a record of the examination findings should take at least half an hour, unusually difficult cases much longer.

Haste and carelessness of observation make for most of the diagnostic errors. A waiting room full of patients like an out-door clinic in a hospital where nose spraying and puffing perfumed oil up the nose constitutes a good part of the

routine. It makes me wonder why, instead of having M.D. after a doctor's name he should not write "Doctor X, Nasal Laundry."

It has been said, at any rate in Toronto, that 60 to 70% of the patients who consult a doctor really do not require to see one. It is because of reading the medical columns in the newspapers where someone comes out with a new cure that physicians have described and long since given up.

The more we know of general medicine the less likely are we to be impressed by long tales of great discomfort and ill health by many patients who are unhappy unless they are having something done to their ear, nose or throat. Maybe it would do more good to tell them, after a thorough examination, that there is no need for them to run to a lot of Specialists and have many trivial operations or local applications as their condition does not warrant any apprehension.

Under similar circumstances, an old teacher of mine, in London, often said to his patients, "There is nothing wrong with you of any consequence or requires any treatment so come and see me again on your next birthday, say in six months or a year."

A few Specialists may say that is good psychology but it does not pay rent, it does, however, conduce to a clear conscience.

JOSEPH C. DOANE, M.D. (closing): Gentlemen, I am very thankful for your generous attention and for the courtesy which you have shown me by not being too critical of my paper.

As a further point of illustration, I have seen a patient who is wandering around Philadelphia with an abdominal wall that looks like a checkerboard. He has had many laparotomies performed in some very fine hospitals. He has fixed pupils, which is one of several indications of the presence of cerebrospinal lues which he shows. He wanders into a hospital often at night with a pain in his abdomen and some surgeon tries to remove a gastric crisis therefrom.

Some time ago a friend of mine came over from New York and I showed him a few cases of subacute bacterial endocarditis. Each one of those had a history of some mouth operation like a tooth extraction within a few months. He decided when he went back to New York that he was going to see whether he in the presence of rheumatic heart disease could not have some preventive anti-biotic treatment in those cases, before he extracted their teeth. Soon a little girl came to him from a good family down on Long Island. He called up the family doctor and said, "I see from the history that this girl has had rheumatic fever. She no doubt has a rheumatic heart. Would you like to do anything before I pull these infected teeth?"

He was told, "You pull those teeth and mind your own business. If you don't do it, I will get somebody else to do it."

That is what I call specialty provincialism at the expense of the patient.

Gentlemen, I am highly honored in being here today.

THE NASAL MUCOSA IN THE LARYNGECTOMIZED PATIENTS

FRED W. DIXON, M.D.

NORMAND L. HOERR, M.D. (By Invitation)

AND

JULIUS W. MCCALL, M.D. (By Invitation)

CLEVELAND, OHIO

At birth the nasal mucosa is covered with ciliated columnar epithelium. Various observers in describing the adult nasal mucosa have noted certain areas where microscopic changes have taken place. These areas, called "inactive areas," are found on the anterior tips of the middle and inferior turbinates and the anterior portion of the lateral wall and a corresponding area on the septum.

In these inactive areas the ciliated columnar epithelium is replaced by stratified squamous epithelium. Particles deposited here are removed by traction of the mucous coat covering this area rather than by ciliary activity. It is believed that these inactive areas are produced through traumatism by the inspired air which contains dust and fumes, aided by dryness caused by low humidity. We have all observed these inactive areas in the nasal cavities of our female patients where the face had been freshly powdered before our examination. In these areas the face powder will sometimes remain for one hour.

It is believed that if the humidity of the room is high, the nasal mucosa moist, and the activity of the cilia normal, the danger of a patient contracting an upper respiratory infection is greatly reduced.

Hilding[1] states that "the rate of the mucinous flow varies from the anterior end of the nose, where it is slow, to the posterior portion of the nose, where it is rapid. In the active area the speed may equal

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From the Departments of Anatomy and Otolaryngology, Western Reserve University School of Medicine.

10 mm. in one minute, while in the inactive nonciliated areas the speed may be only a few mm. per hour. The entire mucosal surface of the normal nose may be cleaned in from four to ten minutes."

Lucas[2] states that "the length of the cilia bears no relationship to the rate of flow. The greatest speed is obtained on the floor and the least on the roof of the nose."

Proetz[3] makes the rule that "the streaming is more active in the protected recesses of the meatuses than in the exposed portions such as the edges of the turbinates and the septum."

In examining the nasal cavities of laryngectomized patients, it was noted by one of us (J.M.)[15] that certain mucosal changes had taken place. The breathing space remains approximately the same after laryngectomy as before operation, but the mucosal color has changed from a normal pink to a light purple. The color is similar to the light purple of an allergic mucosa, but the bogginess is absent. These findings may also be seen in the tracheotomized patients where the larynx remains but is obstructed and is no longer an airway. This color change is probably circulatory due to lack of stimulation from the air currents.

After laryngectomy the inactive areas previously mentioned are no longer dry, but are uniformly moist. Since the air no longer passes through the nose, few bacteria are deposited on the mucosa and those that do find entrance are soon swept away. On questioning, almost all patients stated that preceding laryngectomy, they had averaged from one to three colds a year, but that since having the operation, they very rarely have a "cold." They experienced no feeling of mucosal congestion in sudden atmospheric changes. Nineteen of the patients believed that the sneezing act was only slightly below normal. This is probably due to sympathetic stimulation.

To study these changes, 30 laryngectomized patients were examined. The ages of these patients at the time of examination varied from 35 to 75 years. The average age was 57 years. Twenty-eight were male and two were female. These patients had been laryngectomized from three months to eleven years. The average time elapsing since operation was three years.

Examination of the nasopharynx showed a moist mucosa. All stated that they did not have a postnasal discharge. Mirror and cotton tests taken when the patient was breathing, talking and swallowing, showed only a very small amount of air passing through the nose. The sense of smell, according to the patients' testimony, seemed to be almost lost; yet they were able to detect various odors when blown into the nose. When the pharynx was touched with perfumes, and the patient instructed to swallow, he could detect the odors.

Powdered blue chalk placed only on the inactive areas by an ear spoon, appeared in the nasopharynx in 5-18 minutes. The chalk began to move down and backward immediately, giving the impression that these were now active areas. The average time was 9½ minutes. When one considers that these patients were beyond middle age, when secretory powers and ciliary activity are diminished, this would seem to be about normal.

This, in part, corresponds with the findings of Larroudé[4] who reported on five laryngectomized patients who had been operated upon from six months to two years previously. He noted that the inactive areas decreased in size following laryngectomy, gradually changing to active areas. It does not, however, correspond with our findings when he states that "the cilia in the fast zone in two patients operated upon two years previously, gradually lost their activity, requiring thirty minutes for expulsion into the naso-pharynx."

In our series of cases the time required for the chalk to pass from the anterior tip of the turbinate and the anterior portion of the septum to the nasopharynx, seemed to be an individual phenomenon. Several of these patients had been operated upon only three months previously, yet their emptying time was less than four minutes. Three of the patients who had been operated upon eight, nine and eleven years previously, had an emptying time of five, nine and six minutes respectively. Generally, those patients over 70 years of age emptied slowly. Wherever the mucosa was pale and firm, and gave the appearance of dense fibrous tissue, the chalk moved very slowly. Here there was no return to the ciliated columnar epithelium.

The surface temperature of the inferior turbinates tested by the thermocouple varies with the investigator and may depend upon the

instrument used. Cone[5] placed the temperature of the inferior turbinate in the normal person at 32° C., while Monti and Gregorini[6] fixed it at 36° to 36.6° C. In determining the surface temperature of the laryngectomized patient, in comparison with the normal, observations were taken using a UMA thermocouple recently calibrated. The metals used in the thermocouple applicator were one of iron and the other constantan, joined on top by a silver solder lap. The readings were taken on the anterior surface of the inferior turbinate for ten seconds bilaterally. The patient was instructed to open his mouth and not to breathe. One hundred normal patients were tested in this manner. While the oral temperature remained constant, the surface temperature of the inferior turbinate varied in different individuals and with the same individuals on different days. This did not seem to be influenced by humidity or atmospheric temperatures. Our average reading for the normal person was 34° C. In 14 laryngectomized patients, with an oral temperature of 37° C., the surface temperature of the inferior turbinate was 35.2° or 1.2° C. above the normal healthy person. The temperature of the turbinates in the normal persons varied considerably, but in the laryngectomized patients remained fairly constant. This is probably due to the more constant conditions resulting from lack of ventilation in the nose.

When a stream of compressed air, with a temperature of 13° C., was blown for two minutes into the nose of the laryngectomized patients, the mucosa became more pink in color. The surface temperature dropped 5° to 8° C.

We removed specimens of nasal mucosa from the anterior surface of the inferior turbinates on both sides of five presumably normal individuals and 30 laryngectomized patients. The biopsy specimens were fixed in 10% formalin, or in formol-saline, and imbedded slowly at room temperature in celloidin. The sections were stained by a variety of methods for the investigation of the glandular, vascular, and connective tissue elements as well as the epithelium.

Although the boundary line between the stratified squamous epithelium of the vestibule and the typical respiratory epithelium (pseudostratified, ciliated columnar) of the nasal cavity is not a sharp transition, and is often quite variable, most investigators agree

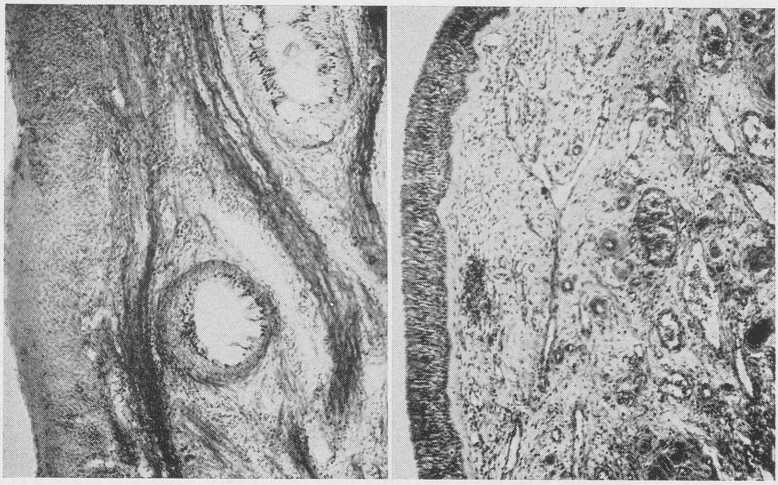


Fig. 1.—Photomicrograph of normal nasal mucosa showing thick bundles of collagenous fibers, and two large ducts from glands deeper in the mucosa; considerable small cell infiltration; stratified squamous epithelium 2 mm. thick. (Mallory's aniline blue connective tissue stain.) (x 100)

Fig. 2.—Photomicrograph of nasal mucosa from laryngectomized patient aged 67, two years postoperatively, showing transitional epithelium, distinct basement membrane, numerous capillaries and veins. (Hematoxylin-eosin stain.) (x 100)

that the anterior surface of the middle and inferior turbinates is covered by stratified squamous epithelium. These surfaces are exposed most directly to the incoming air currents (Proetz,[8] Hilding[7]). Oppikofer,[8] found columnar epithelium on the turbinates, without any areas of squamous epithelium in 17.5% of 200 nasal cavities examined. Schall[9] states that the epithelium of the anterior tip and inferior border of the inferior turbinate in the adult may be frequently replaced by a low cuboidal or squamous epithelium. Schieferdecker[10] describes the anterior end of the inferior turbinate as being clothed by squamous epithelium. These reports agree with the findings of earlier investigators (Henle, Toldt, Ecker, and Zuckerkandl).

In four of the five control specimens we found only stratified squamous epithelium over the anterior surface of the inferior tur-

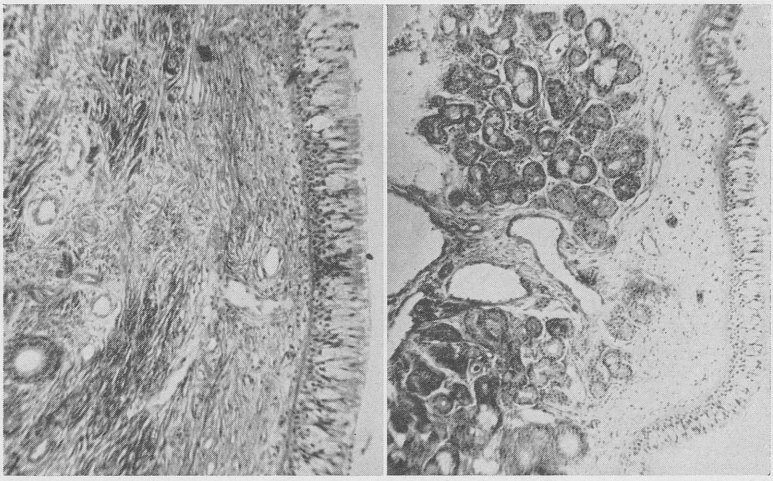


Fig. 3.—Photomicrograph of nasal mucosa from laryngectomized patient aged 38, four years postoperatively, showing numerous mixed glands close to the surface. There is no small cell infiltration in the stroma. Predominance of goblet cells is seen in the epithelium. (Hematoxylin-eosin stain.) (x 100)

Fig. 4.—Photomicrograph of nasal mucosa from laryngectomized patient aged 61, five years postoperatively, showing bundles of collagenous fibers mainly parallel to the surface. (Mallory's stain.) (x 125)

binate. In one specimen there is transitional epithelium and typical ciliated columnar "respiratory" epithelium (Fig. 1 and 5). The squamous epithelium varies greatly, but averages 1-2 mm. in thickness. The stroma is rich in rather dense bundles of collagenous connective tissue fibers, and the glands have large ducts leading to the surface. The subepithelial connective tissue is densely infiltrated by numerous small round cells, mainly lymphocytes and plasma cells. There is an excessive capillary network immediately under the epithelium and, subjacent to this, numerous large muscular veins.

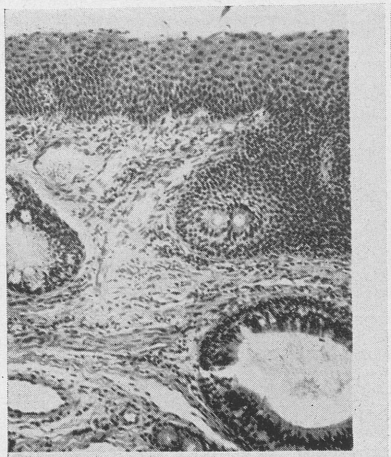
In contrast to the normal, the mucosa of 29 of the 30 laryngectomized patients has a ciliated, pseudostratified columnar epithelium, only one specimen having epithelium of the transitional type (Fig. 2). There is very little infiltration of small round cells and the connective tissue stroma is much looser, with no large dense collagenous bundles as in the normal.

The nasal mucosa of the anterior tip of the inferior turbinate after laryngectomy falls into one of three types, the glandular (Fig. 3, 8, and 11), the vascular (Fig. 2, 7, and 9), or the fibrous type (Fig. 4, 6 and 12). In the glandular type there seems to be a proliferation of racemose mixed mucous and serous glands quite close to the epithelial surface, although this change may only be due to a loss of the dense stroma of collagenous fibers.

In the vascular type of mucosa, there are numerous capillaries immediately subjacent to the epithelium, as in the normal, but the large veins or venous sinuses apparently are much closer to the surface. Unlike the deeper veins of the normal mucosa, which have heavy longitudinal muscle coats, these large superficial veins of the laryngectomized patient (Fig. 7 and 9) have a thin muscle coat.

In the fibrous type of mucosa after laryngectomy, there may occasionally be bundles of collagenous fibers tangential or parallel to the surface (see Fig. 4) but these are never so dense as in the normal. The stroma is made up largely of small bundles of delicate collagenous fibers, not only in the fibrous type but in all the laryngectomized patients. Another finding is the richness of elastic connective tissue. With Verhoeff's hematoxylin stain for elastic fibers, the subepithelial stroma after laryngectomy is found to contain numerous elastic fibers (see Fig. 12), and often a layer of elastic fibers parallel to the surface and just below the basement membrane. In the normal, the elastic fibers are richest around the glandular alveoli, as they have been described (Kubo[11-12]).

We have found some correlation of the histological type of the mucosa with its clinical appearance, the pale or pebbly mucosa tending to be of the fibrous type (Fig. 4), the purple mucosa tending to be of the vascular type with dilated veins (Fig. 7), and the pink to normal colored mucosa tending to be of the glandular type with good vascularity (Fig. 11). There seems, however, to be no correlation which we can discover between the histological structure and age of patient, length of time after laryngectomy, or the ciliary motility. The fibrous, less glandular type of mucosa is found in the older patient, but this is to be expected (Figs. 2, 4, 6, and 12). There seem to be more glands in the younger patients, as is to be expected (Fig. 3, 8, and 11). But the change in the epithelium occurs within



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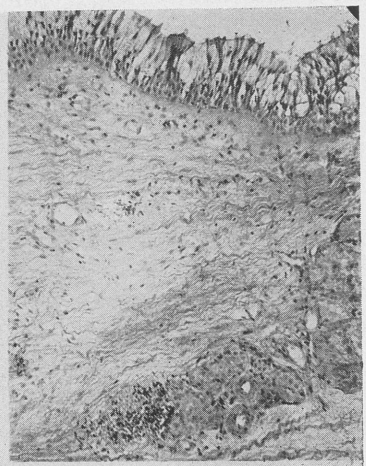

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Fig. 5.—Photomicrograph of normal nasal mucosa, showing dense infiltration of stroma by lymphocytes, plasma cells, and occasional polymorphonuclear leucocytes with rare eosinophils. The epithelium is 1.5 mm. thick. (Hematoxylin-eosin stain.) (x 155)

Fig. 6.—Photomicrograph of nasal mucosa from laryngectomized patient aged 66, two years postoperatively. Fibrous type of stroma shows individual collagenous fibers. There is very little small cell infiltration. Ciliated cells predominate in the epithelium. (Iron hematoxylin and thiazin red stain.) (x 155)

Fig. 7.—Photomicrograph of nasal mucosa from laryngectomized patient aged 67, five years postoperatively, showing loose stroma, and numerous large dilated veins. (Mallory connective tissue stain.) (x 155)

Fig. 8.—Photomicrograph of nasal mucosa from laryngectomized patient aged 35, three months postoperatively, showing glandular type of mucosa; low epithelium, with cuboidal cells in some areas, but mainly ciliated. (Hematoxylin-eosin stain.) (x 155)

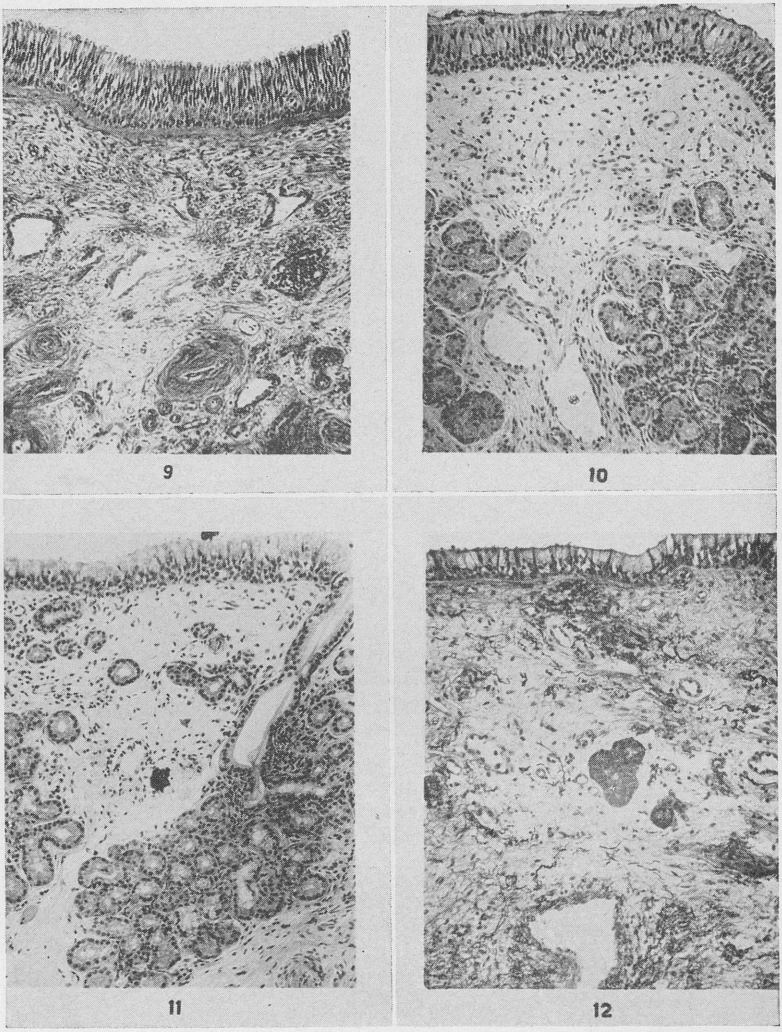

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Fig. 9.—Photomicrograph of nasal mucosa from laryngectomized patient aged 67, two years postoperatively. The epithelium has almost no mucous cells, consisting almost entirely of tall, columnar ciliated cells. The basement membrane is very distinct. Some small cell infiltration is seen. (Hematoxylin-eosin stain.) (x 155)

Fig. 10.—Photomicrograph of nasal mucosa from laryngectomized patient aged 38, four years postoperatively, showing distinct mucous blanket on tips of cilia and practically no small cell infiltration. (Hematoxylin-eosin stain.) (x 155)

Fig. 11.—Photomicrograph of nasal mucosa from laryngectomized patient aged 46, one and a half years postoperatively, showing glandular type of mucosa. Mucous cells predominate in the epithelium. There is no small cell infiltration. (Hematoxylin-eosin stain.) (x 155)

Fig. 12.—Photomicrograph of nasal mucosa from laryngectomized patient aged 74, two years postoperatively, showing elastic connective tissue fibers. The small, slender, twisted black threads throughout the stroma are elastic fibers. (Verhoeff's hematoxylin stain.) (x 155)

three months after laryngectomy (see Fig. 8) and the shortest emptying time was found in one of the oldest patients five years after laryngectomy (see Fig. 7). Neither have we found that the mucous goblet cells predominate over ciliated cells (Proetz) after laryngectomy. Nor can we establish any rule for the thickness and density of the basement membrane, according to Shambaugh's theory,[13] although the basement membrane seems to be most distinct in the older patients (see Fig. 7 and 9).

There is, however, one histological finding which may possibly be correlated with our clinical experience that laryngectomized patients seldom have head colds. In the subepithelial stroma, there is in most of the 57 specimens from 30 patients examined an almost total absence of small cell infiltration, in startling contrast to all the specimens from nonlaryngectomized individuals we have studied.

Sternberg,[14] who studied histologically the nasal mucosa postmortem of seven patients with total extirpation of the larynx, also reported that the lymphoid elements of the mucosa diminish. He stated that the longer the period of time which had elapsed after laryngectomy, the fewer leukocytes, lymphocytes, mast cells, and other wandering cells were to be found. In our investigation, these infiltrated elements disappear to a large extent within the first year after laryngectomy.

Sternberg[14] also stated that the lymphocytes and plasma cells which are normally present in and around the alveoli of the subepithelial glands disappear after laryngectomy. Our findings agree completely with this statement (see Fig. 3 and 11).

We cannot, however, agree with Sternberg's conclusion that the nasal mucosa has a diminished vascularity after laryngectomy, the small vessels gradually acquiring a constricted lumen. Perhaps the difference in our studies is that Sternberg studied only postmortem specimens from patients who had died from recurrence of carcinoma, whereas we studied biopsy specimens removed without anesthesia or vasoconstriction.

We have commented above that although goblet cells are numerous in the surface epithelium, they do not predominate in most

cases over the ciliated cells, as contrasted with Sternberg's report. We do agree, however, with his conclusion that the crescents of Giannuzzi apparently increase in number in the mixed racemose glands of the stroma (see Fig. 3 and 8). Clinically, the mucosa of most patients was quite moist, with a good mucous blanket, and this finding is confirmed by the histological picture of adequate glandular development, with active secretion microscopically.

SUMMARY

1. In the laryngectomized patients the inactive areas gradually become active, the squamous epithelium is replaced by ciliated columnar epithelium and is always moist.

2. The emptying time from the anterior end of the turbinates to the nasopharynx is accelerated. Microscopically, the mucosa is well ciliated, has good glandular activity and a good blood supply.

3. The color change is from a pink to a pale purple.

4. The patients are subject to infrequent colds. Microscopically, there is little or no small cell infiltration.

5. The average surface temperature of the turbinates is higher and more uniform than normal.

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DISCUSSION

JULIUS MCCALL, M.D.: In the post-operative care of these patients, we noted they did not develop head colds. On examination of nasal mucosa, the entire nasal mucosa was moist. The purple color of the nasal mucosa began to appear in some patients as early as two months after operation. When we began to correlate the color of the mucosa with the microscopic findings, we noted a variation depending upon whether glandular or fibrous tissue was found in the submucosa of these patients. After laryngectomy there were fewer sinus infections. Several patients developed cough. Transillumination and x-ray examination revealed a cloudy sinus without symptoms referrable to the sinus. On irrigation of the sinus there was an unusual milky white return. As the sinus infection subsided the cough disappeared. One patient had several large nasal polypi. These polypi without treatment disappeared after operation. Why these people have a relative immunity to head colds we can only offer a theory which may or may not stand the test of further study. It is generally agreed that for infection to occur there must be first, an adequate number of organisms present; second, they must be of sufficient virulence; third, they must have a lowered resistance of the host; and fourth, there must be a portal of entry for the invading organism. In normal breathing, the currents of air passing to and fro from the nose slow up the ciliary activity and dry up the mucous surface causing breaks or cracks in the continuity of the membrane. The slowing of ciliary activity allows a sufficient number of organisms to collect in the breaks in the membrane and begin an infection. People who breathe through a tracheal stoma do not have these currents of air passing through the nares producing these phenomena so there is no portal of entry for the organism.

HAROLD I. LILLIE, M.D.: In the middle twenties, when two-stage laryngectomy was the operation of choice for malignant lesions of the larynx, Stark and I made some observations on the noses of patients who had undergone the preliminary tracheotomy. It was observed that immediately after tracheotomy the nasal mucous membranes were very much congested, and that this congestion disappeared without treatment of the nose in the course of a few days. There was no clinical evidence that this congestion was due to acute rhinitis. The congestion was explained by us on the basis of physiologic activity of the nasal mucous membrane. That is, the air streams no longer were conducted through the nose to the lungs, but passed through the tracheal stoma. After a period of adaptation, the interior of the nose became inactive. The usual swelling of the nose on physiologic demand was absent. This physiologic phenomenon previously had been explained on the basis of acute rhinitis, and the secondary operation for removal of the larynx was deferred until the rhinitis had subsided.

Observations concerning 1 patient were very interesting to us. The patient had complained for a long period of offensive crusting within the nose. On occasion the crust needed to be removed manually. The condition did not appear to be primary atrophic rhinitis, but one very similar to it. After the seventh day following tracheotomy, during which period the patient breathed through the tracheotomy tube, crusting in the nose did not occur. This phenomenon was explained on the basis that because there was no further need for the air currents to pass through the nose, the secretions in the nose were not affected in the drying process that had produced the crusting.

ARTHUR W. PROETZ, M.D.: Not very long ago I spent a very instructive afternoon with Dr. Dixon, and in the laboratories, with Dr. Hoerr examining these specimens, and I was impressed with one point in particular, namely, that specimens from patients 50, 60, and 70 years of age were just as normal as though taken from the newborn. They were textbook pictures of normal mucous membranes with ciliated epithelium everywhere.

This faculty of recovery is a thing I have been stressing for years on much slimmer evidence than Dr. Dixon has here. Jonathan Wright stressed it before me. I believe Dr. Dixon's is a fundamental observation which, if followed up, will have great influence on our management of infectious conditions in the nose.

How the membrane is to be put at rest in patients who have not had tracheotomy remains to be seen. Shutting off the air stream by plugging is not enough. Inflammatory obstructions, atresia, polyps and so on shut off the air streams, but obstruct the drainage. Whether some prosthesis can be devised whereby a comparable situation could be maintained over a period of weeks or months is problematical. Nature is capable of handling the situation, if one can supply favorable conditions.

ANDREW A. EGGSTON, M.D.: As pathologists we have that enviable position that by necessity we must be interested in general medicine and general pathology. Sometimes we do things because we have to do them, but undoubtedly, knowing general pathology aids one a great deal to understand specialists. Unfortunately too many general pathologists don't have the opportunity to see and study special pathology of the ear, nose and throat. Sometimes that is the pathologist's fault and sometimes it is the fault of the surgeon who does not submit the material in proper form. The thing which surprises me in Dr. Dixon's paper is that there is so little change in the nasal mucous membrane when the current of air no longer goes through the nose.

The mucous membrane of the nose is subject to distinct epithelial metaplasia. It does not take much to make the nasal mucous membrane change from a ciliated epithelium to a stratified squamous or transitional type. My own observation is that there is more of the transitional type on the turbinates than on the lateral wall.

In the study of nasal mucous membrane, and I am sure this particular problem was considered, one must stick to a certain location or area for comparative studies because the number of glands, the character of the blood vessels and the character of the surface epithelium varies in different parts of the nose.

I want to bring out the question too, that in submitting specimens to the pathologist, he is often confused because he knows very little about the source and the histology of the nose and sinuses. There is one other thing which I want to emphasize, and that is to indicate any clinical data that is recognized, if the patients were allergic, and if there was an increase in the eosinophiles. I have gotten to the point where I believe that plasma cells and reticulo-endothelial cells are as much an indication of allergy as eosinophiles. Allergy is associated with hyperglobinemia. Plasma cells are also associated with that. With an experimental induction of allergic reaction in tissues you nearly have just as many plasma cells as eosinophiles, and I think one can evaluate these reactions.

I am very grateful for this paper and I think it is a fine contribution that these men made to study the nasal mucous membrane in laryngectomized patients.

FRED W. DIXON, M.D.: In regard to the location from which these specimens were taken, they were all taken from the anterior tip of the inferior turbinate. We took them from this area because it is the most accessible, and because it is an inactive area. We did not use any cocaine because this might have disturbed our biopsy material.

I have nothing to add save to thank those who discussed the paper.

BONY STENOSIS OF THE LARYNX

REPORT OF A CASE

NORTON CANFIELD, M.D.

NEW HAVEN, CONN.

Bony stenosis of the infant larynx is rare enough to warrant report of a case in a two-year-old child, who has now been under my care and observation for 16 years. At my first contact with the patient she seemed to present a typical case of severe laryngotracheobronchitis, with slight chance of recovery. At that time, 1933, modern chemo- and antibiotic therapy had hardly started. No similar case has come to my attention in the meantime. The unusual reaction in the larynx, resulting in complete closure, first by edema, then by laryngeal polypi, and finally by well formed osseous tissue, makes the case unique as far I can learn from my colleagues in otolaryngology and pathology.

J. J. M., aged 16½ months, was admitted to the pediatric service in the Isolation Ward of the New Haven Hospital on September 8, 1933. Her chief complaint was choking as the result of a week of acute upper respiratory infection. Dyspnea had been present for two days and because it was gradually progressing, hospitalization was advised.

Physical examination revealed an acutely and gravely ill child with marked respiratory distress, no cyanosis and no disease except in the nose, throat and larynx and chest. Examination of the throat and nose showed swelling of the mucous membrane and excessive, thick, tenacious secretion in the oropharynx. Direct laryngeal examination showed the mucosa to be acutely inflamed with thick mucopus in the pyriform sinuses. The larynx was markedly obstructed by swelling of the mucous membrane so that there was a very small aperture through which the patient was then breathing. It was thought that the child could continue for a short time without relief so she was

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watched for several hours. Temperature was 39.8° C., respiratory rate, 34. Because of diphtheria as a possible diagnosis she was given 60,000 units of diphtheria antitoxin. A few hours after admission respirations became much more labored and it was obvious that an improvement in the airway was mandatory.

The question of a decision between a tracheotomy and intubation was discussed by the pediatric and otolaryngologic staffs. Previous experience with tracheotomies induced the pediatricians to make an urgent request for intubation rather than tracheotomy. To the otolaryngologic staff, the patient seemed so desperately ill that great pessimism was expressed about her eventual recovery with any sort of mechanical relief of her respiratory distress. Because of possible damage to the laryngeal mucosa, tracheotomy seemed the procedure of choice by the otolaryngologic staff but because of the urgent pleas of consultants, intubation was done approximately seven hours after admission.

Reports of the laboratory tests were as follows: The patient was Schick-negative; blood serology by the Kahn method was negative; from the nose and throat, bacteriologic cultures produced staphylococci and mucosus catarrhalis. There were no Corynebacterium diphtheriae from either nose or throat; blood count was within range of normal with only 5,300 white cells per cmm.; the urine was negative. A culture taken from the larynx by means of swab showed hemolytic staphylococcus, Streptococcus haemolyticus, diphtheroids and pneumococci type 6B. Blood culture showed no growth; blood count on the following day showed 6,800 white cells per cmm. on one count and 10,900 on another; tracheal culture obtained later showed staphylococci and Haemophilus influenzae.

The diagnosis was acute influenzal laryngotracheobronchitis. For the first three days following admission, after the intubation tube had been placed, the patient was given supportive therapy consisting of blood transfusions, intravenous glucose and saline hypodermocylses. Her airway was satisfactory for approximately three days, when increased edema in the airway began to decrease the available respiratory lumen. Direct examination at this time showed that the edema was at the level of the epiglottis *above* the intubation tube.

On the evening of the third day, following an infusion, the patient had a violent spell of coughing and the intubation tube was dislodged. Immediate laryngoscopy revealed no evidence of a membrane but the edema had markedly increased in the hypopharynx. Attempt to introduce a larger intubation tube was unsuccessful and a tracheotomy was performed after the intubation had been in place for three days. This afforded immediate relief and the child from then on was able to tolerate a tracheal tube without difficulty. Further supportive treatment was administered by the pediatric service and the patient gradually recovered from the severe infection, which seemed to be overwhelming at the time of her admission.

During the next two months, ten attempts were made to remove the tracheal tube but the patient could not tolerate breathing through the larynx. The possibility of severe infection in the adenoids and tonsils induced us to remove them in an attempt to eliminate a possible focus of infection. This was done six weeks after admission.

On November 22, 1933, three months after the child was admitted, the larynx was examined and found filled with a papillomatous mass. This was removed and microscopic examination showed it to consist of a typical laryngeal polyp with acute and chronic inflammatory reaction (Fig. 1 and 2).

Microscopic Examination: "Preparation is covered by a layer of stratified squamous epithelium which is fairly well preserved. The keratinizing layer is for the most part missing. The spinous layer is broad and fairly well preserved and composed of loosely arranged ovoid cells with centrally placed well staining nuclei. The germinal layer is intact. The rete pegs are short and blunt. The subjacent tissue contains old and recent granulation tissue with many thin walled blood vessels which are engorged and an exudate of polymorphonuclear leucocytes and large and small mononuclear cells. In some places some poorly preserved mucous glands are seen." (Halpert)

During the following seven months while the child remained in the hospital, many unsuccessful attempts were made to remove the tracheal tube. The larynx was dilated from above and from below but at no time was there a large enough aperture through the laryngeal structure to permit even quiet respiration without ensuing

severe cyanosis. It was thought that possibly too much attention was given to the location of the lesion so that a period of strict rest was advised.

On June 11, 1934, nine months after the original admission, direct laryngeal examination showed that there was no opening through the larynx, not even enough to permit the passage of a small bougie. It seemed necessary then to do a thyroidotomy and examine the interior of the larynx to discover the exact nature of the obstructing mass.

I quote from my operative notes: "The cricoid cartilage was apparently normal; however the stenosis was between the level of the cricoid cartilage and the vocal cords. This stenosis consisted of a hard mass and upon further investigation it turned out to be either proliferation of the cartilage or actual bone formation." This piece of bone was removed with a small mastoid rongeur. A blunt ended suction tube was passed down through the larynx and this was used as a guide to assist in the carving out of the obstruction in the region of the stenosis. After the laryngeal aperture was large enough a "silver permanent dilating tube was placed, this was fitted on the upper end of a tracheal tube through which the patient breathed." The bleeding was annoying and it was hoped that epithelialization of the larynx would take place around the silver tube passing through the stenosis (Fig. 3 and 4).

Following is the pathologist's report of the tissue removed at operation:

Gross Examination: "The specimen consists of an osseous fragment of tissue which is roughly disk shaped, measuring 3 mm. in thickness and 5 mm. in diameter."

Microscopic Examination: "The preparation consists of a small fragment of osseous tissue with well formed haversian systems and narrow spaces." (Tennant)

For the next four months the larynx was kept under observation. A continuous tube was in place through the previously stenotic region. There seemed to be some irritation from the silver tube so

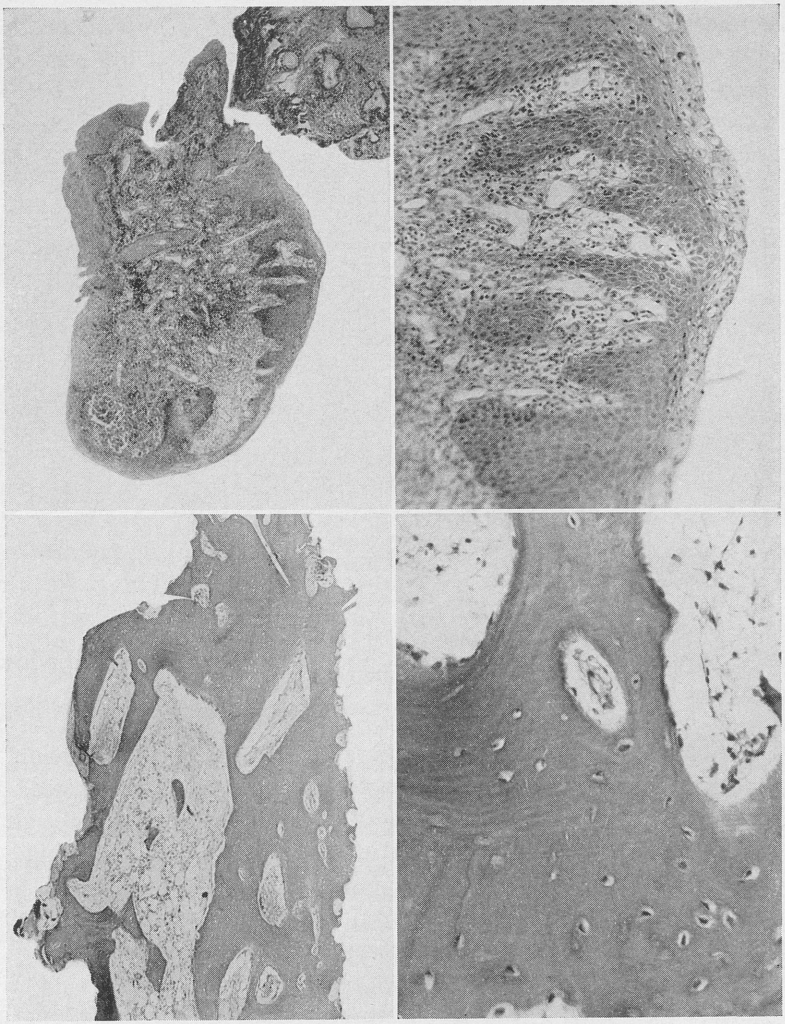

Fig. 1.—Photomicrograph of laryngeal polyp.

Fig. 2.—Photomicrograph of laryngeal polyp (high power).

Fig. 3.—Photomicrograph of bone removed at the level of the stenosis.

Fig. 4.—Photomicrograph of bone removed at the level of the stenosis (high power).

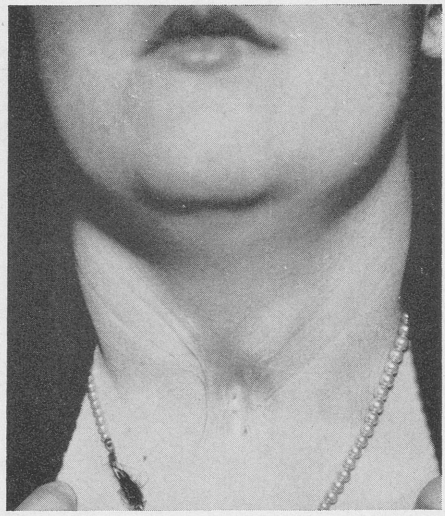

Fig. 5.—Resulting scar 16 years after first tracheotomy.

that it was replaced by a piece of rubber tubing attached to the lower end of the tracheal tube.

On May 17, 1935, 20 months after the original admission of the patient, the tube through the stenosis was finally removed. It was hoped by this time that the child's larynx had grown enough so that it would remain open for satisfactory laryngeal breathing.

The patient was discharged from the hospital on May 28, 1935, 20 months and 20 days after she was first admitted.

Since that time it has not been necessary to replace a dilating tube through the larynx. In the intervening years, however, the larynx has been examined and dilated on eight or ten occasions. In October, 1935, the patient had pneumococcal bronchial pneumonia at which time the scar in the anterior portion of the neck opened and gave her a safety breathing passageway.

The child has developed normally otherwise, her voice has been very hoarse and she has never had a wide open larynx. During her

school years, it was necessary to curtail her excessive activities and she has considered the possibility of a plastic operation on her anterior neck to improve the condition of the scar. Choice between this and an opportunity to be married resulted in the latter, and on October 14, 1948, at the age of 18, she produced a normal male child.

Her voice is entirely understandable and the wound on the anterior portion of the neck is as indicated in the accompanying photograph (Fig. 5).

(The following is what the patient said and reproduced with the wire recorder used at the time of the presentation of the paper.)

"My name is J.J.D.M. and for many years I have had trouble with my larynx. [pause] It started when I was a small child of two years, [pause] and has been a source of concern to me since that time. [pause] However, I have grown up now [pause] and have a fine 7-month-old baby. [pause] My voice is [pause] hoarse but I get along all right." (The pauses noted in the above recitation were where the patient breathed during the short speech.)

The patient's voice as recorded on May 14th, 1949 was presented with a Webster Wire Recorder.

It is interesting to note that at the beginning of her speech she is able to emit many more words during each expiration than she can toward the end. She becomes air-hungry quickly due to the constriction at the level of the larynx. It is also noted that there is an audible wheeze during inspiration. This is always present except during the times of the least necessary oxygen requirements.

SUMMARY

A case of bony stenosis of the larynx in a 2-year-old child, following acute influenzal laryngotracheobronchitis and laryngeal intubation, is presented. The final outcome resulting in an adequate airway for quiet breathing is satisfactory; when more air is required the remaining laryngeal stricture causes an audible wheeze. The voice is markedly impaired.

789 Howard Avenue.

LARYNGEAL STENOSIS

JAMES MILTON ROBB, M.D.

DETROIT, MICH.

Any good textbook on otolaryngology will list all the known causes of the condition we call stenosis of the larynx, which is a narrowing of the cavity of the larynx interfering with the passage of air. For the purpose of this paper a discussion of all the causes and their treatment is impossible; therefore, it shall be limited to laryngeal stenosis following diphtheria, tuberculosis, indwelling endotracheal tubes, indwelling tubes in the esophagus either for feeding or decompression, and accidental crushing of the larynx.

My years of service as Head of the Departments of Otolaryngology in the Herman Kiefer Hospital, Detroit's contagious hospital, in Harper Hospital, a private institution, and in the Receiving Hospital of the City of Detroit, closely affiliated with Wayne University Medical School, have afforded the background for these observations. Fully appreciating that many of you have had more experience with laryngeal stenosis in its various forms than I have, to your knowledge let me add some of my findings that I hope may prove helpful in making the road a little easier for both the patient and the surgeon.

Most of the mild forms of laryngeal stenosis can be relieved by dilatation with varying forms of bouginage. But the severe types seen as a sequel of automobile and airplane accidents with destruction of the entire laryngeal box may bring the most difficult problem seen in all surgery. Then, too, one must not be too sanguine about some of the less severe appearing contractions, for if the mesoderm is in control of the developmental and healing processes of the body giving marked scar formation, difficulties may mount to tax all your ingenuity. We see this situation following tonsillectomy, and I have often said that the healing process that scars and contracts the tissues of the throat following tonsillectomy heals the hernia.

Diphtheria is the most frequent cause of acute laryngeal stenosis, and in its treatment, intubation or tracheotomy, or both, play the chief role. In the contagious hospital of the City of Detroit previous

to World War II, intubation was the first procedure in laryngeal diphtheria with obstruction. In the past several years, tracheotomy has always been performed, and whenever possible this has been preceded by intubation which permits a thoughtful and less hurried tracheotomy. The incompleteness of the records previous to 1927 would not permit a fair appraisal. Therefore I shall present the result of this institution, Herman Kiefer Hospital, for the 21-year period from 1927 to 1947, inclusive.

21-YEAR STUDY OF DIPHTHERIA CASES, 1927 THROUGH 1947

	END RESULTS OF CASES TREATED ON THE SERVICE FOR DIPHTHERIA PATIENTS		
	CASES	DEATHS	FATALITY %
Total diphtheria cases (all types)	8382	842	10.0%
Of the above cases 1073 or 12.8% were the laryngeal form.	1073	211	19.7%
Of the total laryngeal cases 466 or 43.4% were intubated.	466	75	16.1%
Of the total laryngeal cases 59 or 5.5% were tracheotomized but not intubated.	59	30	50.8%
Of the total laryngeal cases 78 or 7.3% were intubated and tracheotomized.	78	38	48.7%
Of the total laryngeal cases 470 or 43.8% were neither intubated nor tracheotomized.	470	68	14.5%

Of all cases of laryngeal diphtheria in which intubation or tracheotomy was performed during this 21-year period, only one case resulted in permanent laryngeal stenosis, a rate of 0.17%.

Out of this entire group there was but one case of chronic laryngeal stenosis, and this was cured in a two-month period at the University of Michigan Hospital with a two-way tracheotomy tube, under Dr. Furstenberg's care. I feel this is a most enviable record, particularly in view of the fact that our lake region produces virulent infections with severe pathological change. My observations convince me that the basis for this almost perfect record is due to the establishment of a call-bell system which summoned any one of a battery of young men consisting of Doctors Donald Young, John Gordon, and Franklin H. Topp with Dr. Benjamin Bernbaum acting as pediatrician through most of this period. The first three, who were in constant service in the institution were all excellent intubationists. Intubation is an art developed only by repetition. The perfection of this art cannot be accomplished today for there are not enough cases to train one's hand. We are therefore seeing another step in the evolution of medicine.

With the advent of good suction, chemotherapy, and antibiotics, and the dwindling supply of expert intubationists, tracheotomy is now the method of choice. Emphasis, therefore, should be placed on a low tracheotomy, properly done, and done sufficiently early so that laryngeal stenosis may not come as a complication.

I have seen cases of panic and spasmodic stenosis in young children. Panic stenosis, an excellent name for it, was relieved when someone conceived the idea of putting a nail through a cork and tying it around the child's neck. This seemed to give him perfect confidence when he put his hand up and felt the cork and tape. A special intubation tube, such as a "non-cough-up tube" or the tube with a long anteroposterior lumen and a narrow neck suggested for spasmodic stenosis, has never been used. Panic and spasmodic stenosis are akin in their development and treatment.

Since at present laryngeal diphtheria is less frequently seen, we are likely to forget that it exists. Let us ever keep in mind that laryngeal obstruction may be laryngeal diphtheria and if undiagnosed is associated with a high mortality. Several experiences in the past year have brought this clearly to my mind.

We have had our difficulties, too. A child aged 1½ years entered Herman Kiefer Hospital with a history of whooping cough severe enough to demand immediate tracheotomy. A hurried tra-

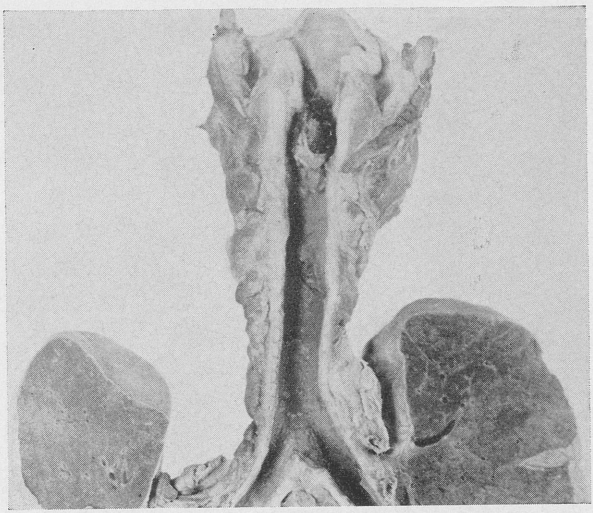

Fig. 1.—Foreign body in larynx.

cheotomy was done, but the child did not do well. A radiographic study of the chest showed pneumothorax of the right lung, areas of consolidation of both lungs, and cervical emphysema. I was called, and a laryngoscopic examination showed an unclean larynx with granulation tissue, mucopus, and edema which I felt at the time was an acute laryngotracheobronchitis. A bronchoscopy was done through the tracheotomy wound, the easy access to the lung, and suction applied. This relieved most of the lung symptoms. When a more complete history was obtained, a peanut episode three weeks before was revealed and further bronchoscopy was decided upon. Unfortunately the tracheotomy tube became blocked and the patient expired. Upon postmortem examination a half a peanut was found in the ventricle of the larynx (Fig. 1). There is only one consolation in the whole episode and that is the pathologist's report: "The material found has the appearance of a half a peanut. It is embedded in loose granulation-like tissue and the surrounding laryngeal tissues are markedly swollen. It is not visible from above or below, and is seen only on opening the larynx."

Now I habitually look for a half a peanut in the ventricle of every larynx I examine, and probably will never find one again.

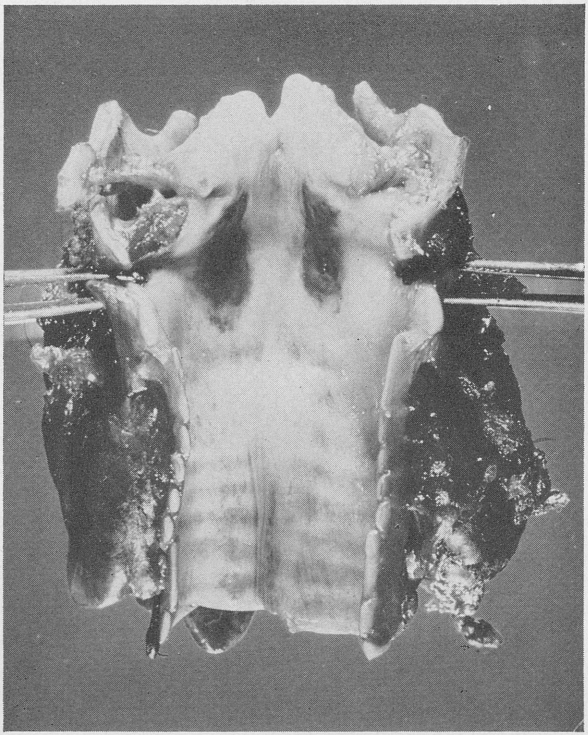

Fig. 2.

Chevalier Jackson's aphorism is most applicable: "Cry over spilled milk enough to memorize how you spilled it."

I have tracheotomized only three tuberculous patients throughout the years. The immediate result in relieving the dyspnea was good, but the soft, succulent, avascular tissue of these patients does not heal well, and in the final analysis little was accomplished. In my experience, if tuberculous larynges heal, they scar with the vocal cords apart and the cavity of the larynx not stenosed, at least in the greater percentage of cases. In this situation, of course, there is a permanent hoarseness. With the advent of streptomycin most cases of laryngeal tuberculosis heal well and apparently permanently providing the lung condition heals so that the larynx is not re-infected.

Fig. 3.—Photomicrograph showing indolent ulceration.

Another step in the evolution of medicine has been the use of endotracheal tubes in anesthesia. To me this has been a great advance in anesthesiology, particularly in long operative procedures. But in its wake, as is true with every advance, come some complications. It has been my experience to have had several cases of permanent damage to the larynx from indwelling endotracheal tubes. One case was that of a young woman 19 years of age, physically well—a case of severe barbiturate poisoning in which a rubber nasal endotracheal tube had been left in place for 30 hours. This was followed by an oral endotracheal tube for 14 hours. As a sequel of this, there was permanent damage to the vocal cords with almost complete destruction of the left cord and considerable damage to the right. In the final healing there was some stenosis, a web formation in the anterior commissure, and permanent hoarseness. A second case was that of a girl of similar age, physically well until she developed an aneurysm of the circle of Willis with hemorrhage into the

brain stem and interference with the respiratory center so severe that she was put in a respirator. An oral endotracheal tube was inserted for 26 hours. It was removed and re-inserted, remaining until the patient's death nine hours later.

Figure 2 is a photograph of the larynx and Fig. 3 shows the indolent ulceration in this case.

Since such cases finally come to the attention of the otolaryngologist he should reach some conclusion as to the length of time indwelling endotracheal tubes should remain before a tracheotomy is considered.

An endotracheal tube may remain for a period of six hours in long operative procedures, and sometimes a bit longer, without any apparent damage—at least no complaint and no hoarseness. The problem, therefore, is how long an indwelling endotracheal tube should remain in place, how large it should be, and of what material? In discussion with Dr. Ivan Taylor, Professor of Anesthesiology of Wayne University Medical School, the conclusion was reached that an endotracheal tube should be removed, cleansed, and oiled, and the larynx examined at least every ten hours. The tube must be large enough to maintain a good airway in a severe anoxic patient. Otherwise, it is not performing its complete function. A No. 32 or No. 34 French catheter is the preferred size for the adult. There is no unanimity of opinion yet whether a plastic tube is better than a rubber one. The plastic tube is inclined to be a little hard and produces in some people an allergic response.

The indwelling esophageal tubes of the Miller-Abbott type next deserve our consideration. Literature provides a sufficient number of cases of chronic laryngeal stenosis following the use of indwelling esophageal tubes to warn us of the dangers of this practice. I have had two patients of this type. One of these had an indwelling esophageal tube left in for a period of two weeks. It was removed at the end of one week and replaced. As a sequel of this, perichondritis of the cricoid cartilage developed with a complete stenosis of her larynx. A thyrotomy was done and an airfoam rubber mold was sutured into the larynx with skin graft covering. The patient developed a most intense inflammation of the larynx and neck. The mold was

removed and a hard rubber mold inserted which did not prove satisfactory. The patient has refused operative procedure of any kind since this experience and wears a tracheotomy tube. Again the problem presents as to how long should these tubes remain indwelling before a gastrostomy or jejunostomy is done? Each case must stand on its own merit but certainly one week should be the maximum in most of them. Of what size should they be? And of what material? The trend of thinking at present is that a tube approximating a No. 18 French catheter, made of rubber is the choice; however, plastic tubes are having some supporters and this group probably will increase in number as the plastic tube is perfected to the point where the danger of an allergic response has been eliminated.

Because of this experience with airfoam rubber I began searching for a very inert substance as a mold in cases of skin grafting in chronic laryngeal stenosis.

Experiment No. 1: Swedish cellulose was implanted in the larynges of two dogs. The result was that both dogs died within seven to nine days postoperatively, from septicemia. There was a severe inflammation around the site of the implant with necrosis of the mucosa and general sepsis. I found out at this time that although tracheotomized humans present a problem in care, they are nothing compared to a tracheotomized dog with its larynx blocked.

Experiment No. 2: In the subcutaneous tissue of a dog was implanted a piece of airfoam rubber uncovered, airfoam rubber covered with a thin finger cot, airfoam rubber covered with goldbeater skin, and a piece of lucite. On the fourteenth day postoperatively, all of these implants, except the lucite, were extruding themselves through the incision. The lucite healed with only a small stitch abscess. Some of the foam rubber molds were sterilized by boiling; others by submerging in 70% alcohol for ten minutes and irrigated with distilled water. The white foam rubber seemed to give the same reaction as the black. It is evident that a special type of airfoam rubber must be used.

Experiment No. 3: We implanted lucite in three dogs—one without skin covering and two with skin covering, and sectioned the

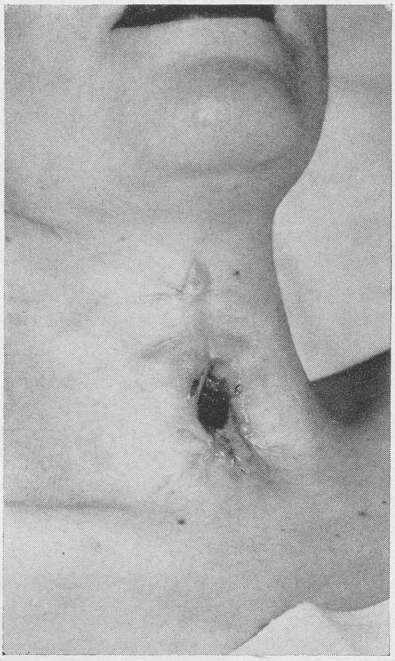

Fig. 4.—Keloid development of skin.

larynges. In two dogs we used penicillin daily, and omitted it in the third dog. Unfortunately, I cannot give good evidence of regrowth of squamous epithelium in the larynx, although I believe this can be done satisfactorily. The dog is an ideal animal for the experiment since it has so much squamous epithelium already within the cavity of the larynx. The following is the report of Dr. Plinn F. Morse of Harper Hospital on the experiments of lucite in the dogs' larynges:

"The sections from the larynges of the dogs present several interesting features:

"1. Differing from the human, squamous epithelium covers the entire area from the tip of the anterior surface of the epiglottis over the false cords and the ventricle and beyond the true cord. Also the section shows beautifully, in a dog, the myxomatous tissue lying be-

neath the true vocal cord which permits the movement necessary for the vibration of the vocal cords.

"2. The ulcerations of the larynx which have been produced artificially immediately present the picture of acute inflammation with a purulent membrane covering the ulcerated surface.

"The dogs that were given penicillin, while they have the ulcerating surface, do not show the polymorphonuclear infiltration of the purulent infection of the original experiments.

"3. There is no evidence that any epithelial graft has taken on the ulcerated surface. There are fragments of squamous and stratified epithelial covering here and there, which are evidently remains of the original surfaces.

"4. In the dogs in which the duration of the experiment was long enough, there is definite evidence of metaplasia of epithelium, the columnar epithelium changing to the squamous type.

"5. In many places the cricoid cartilage has been exposed and in these areas the cartilage is covered by a thin purulent membrane without any attempt at fibroblastic proliferation on the surface. It is evident that the area over the cricoid cartilage is an especially dangerous area and that granulations in this region will not take place unless some special technique can be devised to encourage the formation of granulation tissues.

"6. In one of the young dogs, there is quite active fibroblast formation arising on the cartilage surface from the cartilage itself and it would appear that the capacity of the young animal to heal the lesion was greater than that of the older dogs."

As previously stated in this paper, "Most of the mild forms of laryngeal stenosis can be relieved by dilatation with varying forms of bouginage. But the severe types seen as a sequel of automobile and airplane accidents with destruction of the entire laryngeal box may bring the most difficult problems in all surgery."

Under my care at the present time is a patient who had a crushing injury of her larynx in an automobile accident on November 23, 1947. She has run the complete gamut of tracheotomy, repeated bouginage, rubber mold, orally inserted acrylic mold, thyrotomy with implantation of acrylic mold covered with skin, and still has to wear

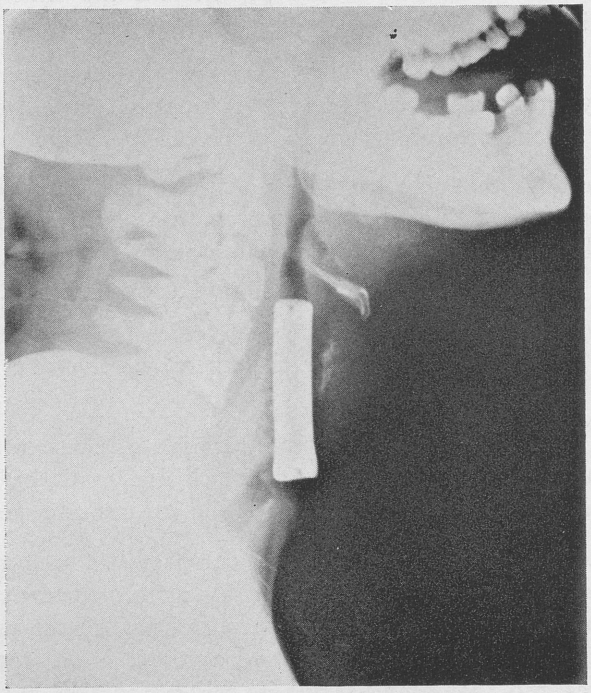

Fig. 5.—X-ray film showing acrylic mold in place.

the mold to prevent contraction even though the skin implant could be clearly seen at both ends of the larynx. At present, I intend to leave in place this lucite mold for at least a year and, if possible, at the end of that time remove it to do the plastic operation suggested by New and Erich.

Figure 4 shows the keloid development in her skin indicative of her scar-forming tendency. An acrylic mold infiltrated with barium sulfate (made by Kenneth Corrigan, Ph. D.) is shown by x-ray in this patient's throat (Fig. 5).

SUMMARY

1. With the dwindling supply of expert intubationists, tracheotomy is the choice for treatment of laryngeal diphtheria with obstruction.

2. With the advent of streptomycin, laryngeal tuberculosis with stenosis will be a rare condition.

3. Severely crushed larynges, I believe, will remain always a serious condition for the laryngologist.

4. With the increasing number of patients using both indwelling endotracheal tubes and also indwelling esophageal tubes, a knowledge of their possible damage is imperative. My conclusions as to the size, the length of time these tubes should remain indwelling, and the material of which they should be made have been given. Some agreement among us on these three points would be helpful as a guide to the profession.

I wish to acknowledge the helpful suggestions of Plinn F. Morse, M.D., and Kenneth Corrigan, Ph. D., of the Research Laboratories of Harper Hospital.

641 David Whitney Bldg.

DISCUSSION ON PAPERS BY CANFIELD AND BY ROBB

Burt R. Shurly, M.D.: I am very proud of Dr. Robb and Harper and Keefer Hospital, where I have enjoyed these many years of practice.

The interesting story of laryngeal diphtheria is fast fading away, but in the earlier days for three years I did more than 500 intubations mostly in private homes. I also had the opportunity of using the first Parke-Davis antitoxin and the first German antitoxin which came to our city. I have watched the story of the fading of intubation and the lack of opportunity for our younger laryngologists to learn this method.

Among those 500 intubations I had 12 retained intubation tubes, which were a source of great trial and tribulation as they always are. We relieved the stenosis in all those cases finally by putting in smaller tubes and by using alum and silver salts on the tube left in place and gradually we succeeded in getting rid of the intubation tube.

This new modern progressive therapy which is available to the profession has given us wonderful results for patients in contrast with what they went through in those early struggles with syphilis, tuberculosis and laryngeal diphtheria. We are happy today to have lived to hear the story of what the medical profession has done for the people of the world.

The problem of laryngeal stenosis, of course, is always one that requires constant alertness. The picture changes so quickly that we must have well trained young men on the alert continuously for observations of the changes which take place.

PAUL H. HOLINGER, M.D.: I should like to ask Dr. Canfield whether the x-rays of the larynx of his patient showed the ossification which was apparent on the photomicrograph and whether that ossification continued into the trachea or involved only the larynx.

Dr. Robb has chosen as his subject one of the most difficult problems in all of otolaryngology and has added a great deal towards its solution. He stressed the "patient factor" a tendency towards scar tissue and even keloid formation as an important part of the etiology of chronic laryngeal stenosis; that is a concept that bears further investigation.

In regard to feeding-tube ulcer of the larynx which goes on to stenosis, I wonder whether it is actually a question of the duration the tube is in place or whether some other factor is responsible for the ulceration and subsequent stenosis of the larynx. In our cases there was no correlation between the duration the feeding tube was in place and the developement of the ulceration. The important feature was the position of the tube. If the patient complains of pain on swallowing or pain in the ear, the larynx must be examined; if edema is present the tube should be taken out or changed; if it cannot be taken out it must be moved from one side of the pharynx to the other by means of curved laryngeal forceps under mirror guidance, anesthetizing the larynx if necessary.

Dr. Robb has presented a series of a thousand cases of intubation for acute laryngeal obstruction with only one case of laryngeal stenosis. This is certainly commendable, and I doubt that this series can be matched anywhere. In discussing this with Dr. Robb, an important fact was noted: the non-cough out tubes were never used. If the child required a larger tube than its regular age should demand because it coughed out the tube, a tracheotomy was done and the intubation was discarded. In seven patients with chronic laryngeal stenosis that we have had under our care, all of whom had been intubated in another institution, stenosis followed either the use of non-cough up tubes or larger than should have been used for the age of that child.

Chronic non-specific inflammatory stenosis was discussed by Dr. Williams and I wonder whether Dr. Robb has seen any of these patients with supra-glottic stenosis that accompany influenzal infections. It was interesting to hear his note about tuberculosis and the fact that there is relatively little stenosis of the tuberculosis larynx as it heals under the influence of streptomycin.

Finally, two types of stenosis which I should like to ask Dr. Robb to discuss are the stenosis following laryngo-fissure which occasionally occurs as a web across the anterior commissure, and that associated with congenital webs. We have had difficulty in keeping both types dilated.

Dr. Robb has presented a very excellent paper on a very difficult subject, and added greatly to our knowledge. I should like to thank him for the opportunity of reading his paper before the meeting and discussing it.

HAROLD G. TOBEY, M.D.: I want to add another point on the indwelling tube—not the feeding tube, but the duodenal tube, the name of which I forget.

DR. ROBB: The Miller-Abbott tube.

DR. TOBEY: Thank you. We have had several instances of ulceration of the esophagus in the region of the cricoid cartilage from the use of this tube which is so small that it is questionable if the ulceration is due to pressure alone.

It was felt rather, that as the tube enters the duodenum, it is subjected to the peristalic tugging of the intestine and this constant motion may be the cause.

NORTON CANFIELD, M.D. (closing): In response to Dr. Holinger's inquiry, x-rays were not taken before thyrotomy as we did not suspect that this might be bone in this patient's larynx. At the time of thyrotomy the bony portion which we removed was confined to that portion of the airway between the cricoid and vocal cords. The rest of the larynx was quite normal. The opening has remained the same since that time.

One other remark about laryngeal edema in cases where an indwelling esophageal tube is used. I believe that the injury is due to the tonus of the cricopharyngeus muscle rubbing the mucosa against the posterior wall of the cricoid rather than the actual size of the tube. A new collapsible tube has recently been used to avoid this complication. This collapsible tube permits the passage of food and avoids undue pressure on the esophageal mucosa. It also has the advantage of preventing any regurgitation through the tube itself because it is collapsed most of the time.

JAMES MILTON ROBB, M.D. (closing): I want to thank all of the discussants for their interest in this subject. Dr. Burt R. Shurly's experience, through the years, of going from one home to another and doing intubations is extremely interesting. It is remarkable also that such satisfactory results were obtained.

I only wish that I could have had Dr. Paul Holinger present to take a picture of the skin implant in the larynx. As my memory serves me I have never seen a congenital stenosis of the larynx.

I believe at present the indwelling acryllic mold is the best material to be used in chronic laryngeal stenosis.

I feel definitely that we laryngologists should interest ourselves in the problems presented by the use of indwelling endotracheal tubes and esophageal tubes and come to some agreement to the end that the best results may be obtained.

CONTRIBUTION OF OLDER FELLOWS

In response to a letter the Active Fellows designated what, in their opinion, was the outstanding contribution to Laryngology of each of those living Fellows who joined the Association prior to 1920. They, in turn, were requested to respond, indicating what motivated them in this particular endeavor.

The following responded:

Harry A. Barnes, M.D.
Ralph Butler, M.D.
George M. Coates, M.D.
Joseph L. Goodale, M.D.
Joseph B. Greene, M.D.
Thomas H. Halsted, M.D.
Chevalier Jackson, M.D.
Harris P. Mosher, M.D.
Francis R. Packard, M.D.
Burt R. Shurly, M.D.
George B. Wood, M.D.

Response of Dr. Harry A. Barnes

My monograph on the tonsils was first published in 1914. It was the result of several years of study in the laboratory of the lymphoid tissues in general and the tonsillar ring in particular. The first half of the book was devoted entirely to the embryology, development and histologic structure of these tissues, both in the normal and in various pathologic states. In the second half I attempted to apply the knowledge gained in the laboratory to the everyday problems of diagnosis and treatment. The book was rather cooly received in this country; being either entirely ignored, or criticized for its conservatism on the question of focal infections and tonsillectomy as a cure-all for the ills that seemed to fit into that category. I did not consider this criticism quite just. Indeed, the book laid stress on the benefits of tonsillectomy. It was, however, a mild protest against that operation for almost every conceivable reason under the sun, and often for no reason at all other than that the patient still had a pair of tonsils that might be removed. I wonder if time has vindicated me on this count; and if so, whether my book has had any influence in modifying that mania for operating that certainly existed even up to the time when I retired from practice (1938).

When I began to turn my attention to malignancies of the sinuses in 1917 the number of cures of carcinoma of the antrum was very low; while the same lesion involving the ethmoid or sphenoid was almost universally considered inoperable. In the few cases that were operated on, local recurrence invariably took place within a short period after operation. These patients were then subjected to a more or less prolonged series of treatment by irradiation, which had little or no effect on the progress of the disease. It occurred to me at that time that if irradiation were given immediately following such minute fragments of tumor tissue as might be left after a careful exenteration would then be most vulnerable to its effects. So I tried this on a most hopeless case of epidermoid carcinoma involving the right antrum, ethmoid and sphenoid, the septum and alveolus and palate of that side. The result was miraculous; for this patient was alive and well 20 years later, the last year of my "follow-up." I believe this was the first time that immediate post-operative irradiation was either suggested or tried on cancers of any sort or in any situation. I have since followed this procedure in upward of 100 cases. In 1927 I reported to the A. L. A. my results on the first 25 of these. If I remember correctly, 42% of the epidermoid carcinomas were alive and without evidence of recurrence after 5 years. The sarcomas (with the exception of the lymphomas, which were hopeless and I am afraid still are) gave an even better result (75%, I think). The follow-up in all of these was very careful and exhaustive; a work, by the way, that is much more laborious and time-consuming even than the treatment of the patient. It is a case of Mohamet going to the mountain in many instances.

Harry A. Barnes.

Response of Dr. Ralph Butler

In reply to your letter, I was influenced in teaching by Dr. B. Alexander Randall, with whom I was associated for twenty-five years, and by my studies in Vienna and Berlin.

When I was appointed Vice Dean of Otolaryngology in 1918 in the new Graduate School of Medicine, University of Pennsylvania, I found myself in the midst of the formation of a new school. The enthusiasm of my colleagues and students stimulated me in carrying on this work until I resigned on account of age in June, 1946.

Ralph Butler.

Response of Dr. George M. Coates

On the day before I finished a two-and-one-half-year internship in the Pennsylvania Hospital in 1901 I expected to go into general practice for a few years, and then possibly decide between pediatrics and general surgery. I was only sure of one thing—I was not interested in either otology or teaching. On that day Dr. Francis Packard told me he was holding a chair for me in the ear dispensary of the Hospital, where he was Chief, and I could start at once. I was flattered, and did so. When he was appointed Professor of Otology in the Philadelphia Polyclinic and College for Graduates in Medicine six months later, he took me along with him, later to become instructor, associate and finally professor, still in otology. To Dr. Walter Roberts, then associate and later professor, as well as to Dr. Packard, I owe much of my later interest in and enthusiasm for both of the fomerly despised subjects.

The courses at the Polyclinic, as in all other similar institutions of the time, were for only a few weeks, and consisted mainly of clinical instruction in the dispensary. Being an instructor in a subject of which I knew little, and had less experience, it was soon evident to me that study, long and hard, was necessary, and that disease of the ear was, after all, most interesting. Being diffident and self-conscious, these characteristics had to be overcome, and the rare didactic lecture, while frightening, was a help. Gradually acquiring knowledge, it became a thrill to help others do the same. I found that the greatest incentive to learning was the necessity of study and preparation before attempting to teach others. Furthermore, the friendships made with the students, both then and now, have always been one of the great rewards for teaching classes of both undergraduate and graduate students. Friendship aside, it is most interesting to follow the careers of one's former students, to see them develop into capable otolaryngologists, rise to high hospital and teaching positions, become fellows of the more advanced special societies, and finally to hold high office. That, I think, is what makes teaching, especially graduate teaching, a thrilling part-time occupation or avocation.

When it was evident that the old six weeks' courses for specialists were far from being adequate, I had a part, in about 1915, in organizing a regular schedule, capable of being expanded, for courses of much longer duration and including regularly scheduled

didactic teaching and clinical instruction in the operating room and wards, as well as in the out-patient department, our idea being to extend the course to four or six months as soon as possible. World War I interrupted these plans, but in 1917 the Polyclinic joined the University of Pennsylvania in forming the Graduate School of Medicine, and our tentative schedule of a few years before was put into operation as a University course. With the arrival in 1919 of our first full academic year class, interest in teaching became at once much more intensive and satisfying, and seemingly more worth while, and this interest has grown from year to year.

During all these years I have found by far the greater proportion of students intelligent, honest, capable and eager to acquire knowledge, and it is with no small satisfaction that the teacher feels that he has been helpful in starting hundreds of bright young men on the high road to successful achievement, and that, although he may not remember all of them, he has hundreds of friends and well-wishers.

This is the way, and these are the reasons, I became interested in teaching—pure luck at the start.

George M. Coates.

Response of Dr. Joseph L. Goodale

It is not altogether easy to answer the query in your letter of Novembes 15, but perhaps a brief chronological resume will serve the purpose.

Early life in a scientific atmosphere: grandfather, S. L. Goodale, chemist; father, G. L. Goodale, professor of botany at Harvard.

In 1894, bacteriology at Heidelberg.

In 1894-95, preparation of diphtheria antitoxin for the Massachusetts State Board of Health.

Observation of shock in certain individuals following administration of antitoxin.

Correlation of this fact with experiments on persons suffering with horse asthma.

Studies of the phylogenetic tree of plants in relation to hay fever and asthma from 1912 on. After this date my own work and that of others brought a rapid expansion of our knowledge.

I may perhaps mention that some remarks, which Theobald Smith made to me sometime in the nineties, regarding the sensitization of laboratory animals, were only later brought into significant relationship with hay fever and asthma.

Joseph L. Goodale.

Response of Dr. Joseph B. Greene

In 1909 while living in Birmingham, Alabama, my wife, who was a victim of pulmonary tuberculosis, developed laryngeal tuberculosis. Naturally, I became vitally interested in this complication and moved to Asheville, a tuberculosis center. From that time on much of my professional work was devoted to the treatment of tuberculous laryngitis.

Joseph B. Greene.

Response of Dr. Thomas H. Halsted

In 1906, Killian of Germany was invited by the American Laryngological, Rhinological, and Otological Society to read a paper on esophagoscopy and bronchoscopy and to demonstrate his method of entering the esophagus and bronchi. I was present at that meeting and, looking back over forty-odd years, I think it was his clear, competent demonstration that gave me the first motivation to go and do likewise. A year later, Chevalier Jackson of Pittsburgh gave a demonstration before the same Society of his modification of Killian's method, the chief difference being that while Killian's light was on the proximal end of the tube, Jackson's was at the distal end and smaller. It would therefore lie at the very site of the object to be seen and of the foreign body if there were one. I was deeply interested and made a definite resolution to utilize Jackson's method whenever the next case that warranted it came into my care. A few months later, the opportunity presented itself. In October, 1907, Dr. Stockton of Buffalo sent me a little boy of five years of

age, saying that the child had a congenital stricture of the esophagus which would need continual bougeing.

I advised an x-ray, feeling that it would be extremely hazardous to pass bougies without more definite knowledge of the site of the stricture and dilatation. Roentgenology was then in its infancy and there were no facilities for it in any one of the 4 hospitals in our city, but a fluoroscopy revealed a round object, resembling a quarter of a dollar, opposite the fourth or fifth vertebra.

The diagnosis was settled, the treatment was not. Finally, however, the boy was anesthetized at Dr. Coon's office, the fluoroscope turned on, and I passed a long alligator forceps, 18 inches long and covered with rubber tubing, down the esophagus, until the biting edge was opposite the foreign body. I was unable to grasp anything and it became apparent that the object was encysted in the wall of the esophagus. Jackson's method was clearly indicated but I had first to obtain the instruments. I did so, and spent 3 weeks familiarizing myself with them.

The family doctor refused to associate himself with what he considered my almost homicidal plan but the parents consented, so finally, in November, 1907, I operated on the child under ether anesthesia. I could not find or feel the coin. Fearing hemorrhage, I hesitated to use the curette I had had made for the purpose from to spokes of a bicycle wheel welded together. The instrument was about 30 inches long. After trying for an hour to locate the coin, I finally used this instrument and after a few minutes succeeded in scraping through the mucous membrane, which was really scar tissue, and brought the edge of the coin to view. In silence I drew it out with the tube forceps—a one-cent piece. I could not speak, the strain had been so great, but there was a great release of emotion around me and a great spontaneous clapping of hands by the 20 doctors in the operating room. That operation took over an hour and today it would be done in ten or fifteen minutes. The coin, which had lost 1/8 of its original weight, had been swallowed when the child was only five months old or younger.

This case was first fully reported at a meeting of this Society at Montreal in May, 1908, in a paper entitled "Personal Experience in the Use of the Bronchoscope, Esophagoscope and Gastroscope, with Reports of Fourteen Cases," later published in the Transactions.

I hope that in this brief paper I have succeeded in giving you a quick picture of my first experiences in the field of bronchoscopy, esophagoscopy and gastroscopy in the early days, when the specialist was unaided by the many modern technological devices now in use.

Thomas H. *Halsted.*

Response of Dr. Chevalier Jackson

Although I had not thought of it before, it seems to me the incentive to the feeble efforts I have made could be summarized in seven words: Hope of lessening needless suffering and mortality. If you deem it worth while to cite details as to forms of avoidable misery and death the following few examples might be mentioned:

1. Many children came to the clinic almost dead of hunger and thirst because household lye was not labelled "Poison," and sodium hydroxide was sold as a cleanser labelled "will not injure the hands or the most delicate fabric."

2. A high percentage of mortality occurred in children as well as adults because of unskilled attempts at esophagoscopy with huge crude instruments. I have never recovered from the shock given me forty years ago when E. Fletcher Ingals said to me: "The mortality of bronchoscopy is 25 per cent; of esophagoscopy 75 per cent; not your mortality, Dr. Jackson, and not my mortality; but the over-all mortality, including that of the man who telegraphs for a bronchoscope or esophagoscope and attempts endoscopy on a baby without ever having looked through an endoscopic instrument before."

3. Many children died of instrumentation at the hands of untrained operators unaware of the avoidable pitfalls of peroral endoscopy. The most frequent of these pitfalls was in the introduction of the esophagoscope and in the pulling of of foreign bodies from the air and food passages with no prior attention to the solution of the mechanical problem involved.

4. Having discovered that over 85 per cent of foreign body accidents were due to carelessness, I carried on a campaign for prophylaxis, for many years.

5. Children with the then prevalent diphtheritic and streptococcic laryngotracheitis were tracheotomized with an average mortality of about 75 per cent, largely due to neglect of the proper aftercare; and about 50 per cent of the survivors had cicatricial laryngeal stenosis because the tracheotomy was done too high, usually a stabbing through the cricoid or thyroid cartilage, or both.

6. Untold thousands of people with bronchopulmonary infections were drowning in their own secretions for want of peroral endoscopic aspirations.

7. There was an appalling mortality from bronchial obstruction due to suppression of the cough reflex (the watchdog of the lungs) by opium, which not only promoted accumulation of secretions but increased the adhesiveness and cohesiveness of the obstructive secretions so they could not be expelled by the normal peroral drainage of ciliary wafting, tussive squeeze and bechic blast.

8. The needless suffering of babies with peanuts and adults with other forms of bronchial obstruction mistreated for asthma, drove me to broadcast the axiom, "all is not asthma that wheezes."

9. Having studied art and having spent much time sketching from nature, I was fascinated with the everchanging form and color of the mirror views of the larynx, and the endoscopic images of the esophagus and tracheobronchial tree. Often the form and color of a foreign body appeared and could be put in, as an artist would put in a human figure in sketching a landscape. Additionally, there was often the thrill of painting the appearances of something that had never been recorded before.

10. In 1938 and prior years, it was borne in upon me that the revelations and accumulated knowledge of the anatomy and physiology of the tracheobronchial tree and esophagus, as well as of the etiology, pathology, diagnosis and treatment of diseases of these regions, justified recognition of Broncho-Esophagology as a department of Medical Science. The first step in seeking this recognition was to call the attention of the American Bronchoscopic Society to the semasiologic solecism of its name, which meant literally a society of "lookers in." The Society promptly changed its name to the American Broncho-Esophagological Association, and Broncho-esophagology is now accorded a proper place as a Department of Medical Science.

I should like to add that any footprints we oldsters may have made in the sands of time will be obliterated by the flood tide of progress in medical science; and credit, *if any*, will go, figuratively, to Amerigo Vespucci, instead of Christopher Columbus. What difference does it make?

Chevalier Jackson.

Response of Dr. Harris P. Mosher

After finishing my surgical internship at the Massachusetts General Hospital I settled in Boston, hoping eventually for a practice in general surgery. As this did not come, I took up Ear, Nose and Throat on the side and finally after about five years went over fully to the specialty. Then I spent four months in Germany, three months in Berlin, and one month in Southern Germany at Halle. In Berlin I took a course in the anatomy of the ear, and a clinical course in Ear, Nose and Throat under Halle, but gave most of my time to Jansen's clinic, where Dr. Canfield, who had been Killian's assistant for a year at least, introduced me. Jansen was the outstanding man at that time in sinus surgery.

After Berlin I went to Schwartze's old clinic, where his successor Grunert gave a postgraduate course on the surgery of the temporal bone. This course was so thoroughly equipped and so well given that I made up my mind if I ever gave a course, it would be patterned after this one.

I came back to Boston enthusiastic about the anatomy and surgery of the accessory sinuses. I was admitted to the Anatomical Department of the Harvard Medical School and at once started a course on the anatomy and surgery of the accessory sinuses, using left-over material from the dissecting room and babies from the Lying-In Hospital. The babies proved splendid for cameo dissections of the face and neck.

Before going to college I found out that I did not have enough talent to become a professional artist, but found out later that drawing was a great help in my teaching.

I had a somewhat new subject to teach, namely the anatomy and surgery of the accessory sinuses. I followed Killian's teaching

as well as I could. Students kept coming year after year, and I soon realized that I liked to teach, that my personality perhaps, helped a bit, and I have been teaching almost without a break for thirty-five to forty years.

At the beginning of my practice of the specialty Killian had just launched bronchoscopy for foreign bodies in the trachea and the lungs. Naturally, esophagoscopy was soon added. As I always liked to do things with my hands, the mechanical side of these procedures appealed to me, and I took up this kind of work. The Medical School again helped by giving material for gross anatomical study of the esophagus, and the hospital laboratory furnished facilities for the study of the pathological conditions of surgical specimens.

Harris P. Mosher.

Response of Dr. Francis R. Packard

After graduating from the University of Pennsylvania Medical School in 1892 I applied for a residency at the Pennsylvania Hospital in Philadelphia. At that time they had but five residents and there was a long wait before taking the applicants. I filled in the time which I had to wait by passing some three months—at the kind suggestion of Dr. William Osler—working in the laboratory at Johns Hopkins. To Sir William Osler I owe the origin and stimulation of my interest in the history of medicine and it was to him that I owe my first contribution to the literature of the subject. I then served as resident for about six months at the Children's Hospital in Philadelphia before assuming my duties as resident physician at the Pennsylvania Hospital. The service was very active, rarely a day in which we did not have at least one tracheotomy or intubation performed. I might recall that at that time we knew nothing about antitoxin.

I served for two years in the Pennsylvania Hospital at the expiration of which time I started in general practice. The Out-Patient Department for Diseases of the Ear at the Pennsylvania Hospital was then associated with the ophthalmological. Dr. George C. Harlan had been the chief of the ophthalmological, laryngolog-

ical out-patient departments for some years. A year or so before he had persuaded the managers to separate the laryngological department and put in charge of Dr. Alexander MacCoy and he had kindly suggested to me would turn the otological department over to me so I got busy. Dr. MacCoy, being in rather poor health not very long after gave up the nose and throat department and the managers then combined it with the department for diseases of the ear and I was put in charge of the whole service. My first article connected with those specialties was "Scarlatiniform Eruptions Following Operation or Traumatism," published in February, 1897, and was followed by others, chiefly clinical articles. I continued to do some general work but my inclination was to get into general surgery. In 1897 I published "An Analysis of Two Hundred and Twenty-one Cases of Foreign Bodies Introduced into the Male Bladder per Urethra, with a Report of a Recent Case." This case occurred in a man whose wife I had just delivered of a child and who took the opportunity, while she was sick, to ask me to deliver him of a watch-chain bar which he had misplaced in his urethra twelve years before.

The following year, 1898, I was commissioned first lieutenant and assistant surgeon in the 2nd Regiment, Pennsylvania Volunteer Infantry and served with it until my discharge from the army the following October. My regiment smelt more powder and saw less fighting than any other in the service as they were at the DuPont Smokeless Powder Works all summer. After my discharge from the army I confined my work exclusively to disease of the nose, throat and ear.

For some years I was Professor of Laryngology and Otology at the Philadelphia Polyclinic and College for Graduates in Medicine and was also Dean of that institution from 1901 to 1906. I was also Chief Laryngologist and Otologist to the Pennsylvania Hospital, Laryngologist to the Children's Hospital, Consulting Aurist to the Bryn Mawr Hospital and Consulting Laryngologist to the Pennsylvania Institution for the Deaf and Dumb, the Eastern Penitentiary, and the State Asylum for the Insane at Norristown.

I joined the Medical Reserve Corps in World War I and sailed on May 19, 1917 overseas with Base Hospital No. 10, United States Army. This unit was attached to the British. I remained with it

until September 1918 when I was attached to the A.E.F. and sent to Paris as Chief Center Consultant in Laryngology and Otology for the District of Paris. I was discharged from the Army on January 25, 1919.

From an early age I had suffered from cacotheses scribendi and in 1901 the Lippincotts published my "History of Medicine in the United States." It went through a second edition in 1931. This was followed in 1908 by my "Text-Book of Diseases of the Nose, Throat and Ear, for the Use of Students and General Practitioners." In 1915 I wrote the Preface to the Gold Headed Cane, by William MacMichael for which Dr. Osler had written the Introduction; and in 1920 published in "The School of Salernum" (the English version by Sir John Harington) "The History of the School of Salernum," also "Life and Time of Ambroise Paré." "The History of the Pennsylvania Hospital Unit (Base Hospital No. 10, U.S.A.) was published in 1921; "Guy Patin and the Medical Profession in Paris in the XVII Century" in 1925; and in 1938, "Some Account of the Pennsylvania Hospital, from the First Rise to the Beginning of the Year 1938." Besides these books I contributed to the current periodical literature and from 1901 to 1906 was editor of the American Journal of Medical Science. From 1917 to 1942 I edited the Annals of Medical History until it suspended publication in November 1942—a war casualty.

Francis R. Packard.

Response of Dr. Burt R. Shurly

Your letter started me thinking back about forty years. At that time when the Detroit Tuberculosis Sanatorium was just established, I had many cases of laryngeal tuberculosis under observation and treatment. Nothing was then known about the vitamin content of foods, but we used what came to be known as "Shurly Soup"—a serving consisted of a wineglassful three times a day. It contained two tomatoes, two carrots, two beets, two potatoes, and a bunch of celery, squeezed and liquidified. This, with milk, eggs, and leafy vegetables, seemed to benefit these patients. This was twenty years before the importance of the vitamin content in foods was recognized. We became greatly interested to know why this diet and "soup" helped, and research work at the Medical College

was started. Under my direction, studies were made of what might be of value in these foods. Monkeys, white rats, and guinea pigs were observed without and with these foods, and before long we saw that a deficiency of Vitamin A gave rise to ulcers of the cornea, ulcers of the tongue, sinus infection, suppurative otitis media, and respiratory infection. These could be cleared up in two weeks with the use of Halibut liver oil, one mm being equal to three teaspoonfuls of cod liver oil. This was reported to the Pacific Eye, Ear, Nose and Throat Society—the first clinical record, I believe, of the use of Halibut liver oil. As this work preceded the era of the understanding of vitamins, it was a contribution to a subject which by now has crowded all medical literature.

Thinking back, too, there were my five hundred intubation cases, with the experimental use of Parke Davis diphtheria anti-toxin, before it was put on the market. You remember that the mortality rate was reduced from 80% to 20% in a period of three years.

As I have said, my interest was aroused by the helpfulness to sick patients of certain foods, long before the vitamin story became the important factor it is today.

Burt R. Shurly.

Response of George B. Wood

As I understand it I have been asked to make a statement in as few words as possible why I undertook the study of the "anatomy and histo-pathology of tonsillar tissue." One must grant that it is often difficult to state precisely the incentive that leads one into a definite field of endeavor. Maybe it is inclination, training, opportunity or just chance. It was perhaps my training at Goettingen in Germany under Professor Aschoff that created a distinct interest in histopathology and I had the opportunity of working in the Wistar Institute of Anatomy of Philadelphia and in the Veterinary School of Medicine of the University of Pennsylvania, the latter for my animal experiments.

In the early 1900's the why and wherefore of the tonsillar tissue of the throat was little understood and the conjectural opinions of the function of this tissue were largely empirical. There were of

course textbook descriptions of the tonsils both gross and histological and in the field of histopathology there was a very able presentation on the pathology of acute tonsillitis written by Dr. Goodale whose findings I was able to confirm in every detail.

However the textbook description of the histology of the normal tonsillar tissue certainly left much to be desired and in certain ways did not coincide with my own findings. From what I saw I could not accept the theory that the presence of lymphoid cells in the epithelial lining of the tonsillar crypts was an infiltrative process from the parenchyma, nor did the various theories concerning the function of the tonsils as proposed at that time fit in with what I saw in the clinic and in the laboratory. The massacre of the tonsils was just then getting off to a good start. Probably four out of every five laryngological operations were tonsillectomies, a bloodletting that was apparently clinically justified in most cases but it did raise a question as to the wherefore of the existence of this tissue. This presented a very pregnant field for further investigation and I thought if by animal or other research I could shed any light on the reason of their existence and use to the individaul it would be a worthwhile endeavor.

From a review of the literature concerning the origin of lymphoid cells I found that while there was little as to the tonsillar tissues themselves there was a great deal of discussion concerning the histogenesis of the thymus gland. There seemed to be a growing belief among histologists who had made a special study of the question that the lymphoid cells constituting the bulk of the fully developed thymus gland originally came from the epithelial anlage and it seemed very possible that the peculiar relation of the lymphoid cells to the basal layers of the cryptal epithelium of the tonsils was an analogus picture. This led me to a histogenetic study of large numbers of pig embryos. The hog was selected because its tonsils are large and very similar in their histology to that of the human faucial tonsil and being placed in the soft palate are comparatively accessible.

The result of this research was the subject of a paper which I read before the American Laryngological Association in 1909 and again formed the bulk of my Presidential Address in 1939, the results of the earlier investigation having been in 1939 confirmed by further research.

In the course of routine histological examination of tonsils both faucial and pharyngeal I found that there was histological evidences of what was apparently primary tuberculosis in about 4% of all tonsils removed, these results corresponding very closely to a careful review of the literature on this subject at that time. Also in a post mortem check on tonsils removed from some 30 patients dying from pulmonary tuberculosis there was in every case histological evidences of this disease in the tonsils. These findings suggested a series of experiments on the pig to determine if the tonsillar tissues were more susceptible to tuberculosis than other portions of the upper respiratory tract and if possible why. It was found that when a culture of living tubercle bacilli was swabbed on the tonsil of a young pig, not only did there develop in every case tuberculous lesions in the tonsil, but also the tubercle bacilli could be recovered from the regionary lymph nodes before the disease had developed in the tonsil sufficiently to be recognized histologically. This was conclusive evidence that the cryptal epithelium was not a barrier to invasion by the tubercle bacillus though histologic studies of the human tonsil seemed to indicate that ordinary pathogens, streptococci, pneumococci, etc., did not gain access to the parenchyma until definite areas of the cryptal epithelium had been destroyed by the invading infection. This raised the question as to the relation of the virulency of the invading organism to the vital resistance of the invaded host, hence the series of experiments on the hog with anthrax bacillus, an organism to which this animal was especially susceptible.

While the material obtained from the tonsil massacre afforded the chance for study of the more chronic tonsillar lesions it was seldom that any acute tonsillar pathology could be observed. A patient admitted to the Howard Hospital with acute suppurative tonsillitis having difficulty in breathing and slightly cyanotic on account of obstruction from the enormous acutely swollen tonsils gave me the material for the histological study of acute suppurative tonsillitis. Not only, as I have already mentioned, was I able to confirm the findings of Goodale but also that the organism gained access to the parenchyma tonsil only after there had been ulcerative destruction of the cryptal epithelium.

The impulse that induced me to make a cadavaric study of the peritonsillar spaces was the clinical fact of the free mobility of the faucial tonsil in the tonsillar fossa, which mobility renders the oper-

ative removal of this organ a comparatively simple procedure. It was hoped by injection of gelatin into the peritonsillar areas to outline the areolar spaces surrounding the tonsil and also the areas of attachment of the tonsillar capsule to the peritonsillar musculature.

To summarize, a duty beholden upon all those who would write on technical subjects, I might say it was both training and inclination plus opportunity that led me to do this particular type of research, the study of "the anatomy and histopathology of the tonsillar tissues."

George B. Wood.

ANALYSES: WHAT LESSONS MAY WE DERIVE FROM THESE

ARTHUR W. PROETZ, M.D.

AND

H. I. LILLIE, M.D.

ACCENT ON YOUTH

ARTHUR W. PROETZ, M.D.

ST. LOUIS, MO.

When Einstein formulated his theory of relativity he was 26 years old. At 26, Leonardo had completed three of his immortal canvasses. At 26, Shakespeare wrote his first play; Edison was 31 when he turned out his lamp. Mozart died at 35.

Packard wrote medical history at 22 while still a hospital resident. The first brew of Shurly's soup poured from its kettle while the young chef's hair was still a raven black. Mosher wrote, in his Semon lecture, " . . . for all my medical life I have been working on the esophagus."

The germ of greatness flowers early.

While it is given to some of the great to think and develop and produce well into the ripest of old age, the shining discoveries which immortalize them are made in their thirties.

It is fortunate for science that the drive which goes with curiosity, original thinking and personal research is irrepressible and survives a deal of stifling; for young genius goes often unrecognized and men reach middle age before their deeds are known.

It happens perhaps more often that discoveries filter gradually into the great mass of scientific knowledge and become important much later when nobody bothers to find out who made them.

Since you, Mr. President, have had the foresight to prevent such neglect of the members of this Association by looking back at their good works, may I have the hindsight to look ahead and peer into the future?

It is interesting to speculate which of us in this company is producing something today which will survive in the practice and teaching of the twenty-first century.

In a world seething with scientific discovery sources are not always traced; origin become obscure and names are forgotten. Only the very great remain clearly delineated.

Of what does this greatness consist?

I have often pondered the lives and characters of men whom we revere and wondered just what set them apart from the crowd.

Surely not a brilliant personality; that is a transient thing: it reflects upon those who come within its circle, fades when that circle vanishes.

Singleness and seriousness of purpose may move mountains but it takes genius to discriminate: which mountains and where. Movement is not always progress.

Education is only a tool; a chart; a design for thinking.

Greatness is an elusive quality, not to be confused with fame. The modest may attain the heights; but so, for that matter, may the blowers of trumpets, for even among the great are some who cannot help making a business of it. They are forever writing letters and diaries and leaving them around for their biographers to discover. They fly to the photographer's flash like a moth to a flame. They write for the magazines and their conversation bristles with the names of V.I.P.'s.

My candidate for the Hall of Fame is one who has curiosity; who has the enthusiasm and the training to satisfy it; who has the intelligence to put what he finds to good use, and the grace to tell the rest of us about it.

The great laryngologists of tomorrow are busy somewhere at this minute with the discoveries which will some day make them great. I hope that they can be ferreted out (if indeed they have not already been) and brought into this Association while they are still young enough to profit by our encouragement, and while we are still young enough to sit at their feet and listen.

So it was with these colleagues whom we honor today. With reverence I salute them.

RENOWN ARISES FROM PERSONAL EFFORT

H. I. Lillie, M.D.

Rochester, Minn.

It has been found difficult to express adequately in words what was felt in my heart. When I was asked by Doctor Hill to summarize the expressed motivation and circumstances under which certain of our distinguished senior members decided to undertake the study of otolaryngology as a career in medicine I accepted the assignment with serious misgivings.

The title of this discussion seems particularly applicable to these distinguished physicians because it is at once obvious theirs was the most difficult period in which to begin the study of otolaryngology. Each succeeding generation of physicians since the time of Aesculapius has contributed much to the progress of medical science and information. The movement has been continuously forward. There is much evidence that the progress made by recent generations has surpassed by leaps and bounds the rate of progress made previously. There are many reasons why the progress has been so rapid. The accumulation of information produced by scientists in general and especially the information adaptable to medicine in particular which has been turned to the use and advantage of the physician has been an important factor. However, it required physicians with foresight and imagination to apply the information to their needs in treating patients.

Among the senior members of this, The American Laryngological Association, the oldest organization of its kind in this country, there are those who have contributed outstandingly to the progress of otolaryngology. In reviewing the short and diffident autobiographies presented for this review it was noticed that much has been omitted that is well known to the profession. Really great men are humble men.

It must be realized that in the formative days of the careers of these senior members of the Association there were few, if any,

organized training centers available for special study in this country. The European clinics offered training but at a considerable cost to American physicians in time and money. Later the organization of the American training centers was patterned after the European centers.

It can be said that our distinguished seniors obtained their training the hard way. More glory for their outstanding achivements and more credit for their fortitude and tenacity of purpose!

It would be well for those of the younger generation to emulate the seniors who overcame such difficulties. It seems that at the present time there are some of the younger generation in training who expect to be spoon fed and make rather exacting demands in the way of opportunities and financial assistance. Perhaps if candidates for training in the specialty were required to read the history of its development, they would realize what a fortunate opportunity they have. Actually there are not sufficient organized teaching centers to accomodate all candidates, but there are many splendid opportunities to improve greatly their knowledge if those desiring training would put forth the effort.

Too many times not enough credit is given to the natural ability of the individual physician who has arrived at the fulfillment of his ambition mainly through his own effort. Such a physician would not be denied the fulfillment of his ambition, and in his heart rightfully feels an increased pride in his accomplishments for this reason. We have the example of our older generation to offer as proof of such a statement.

The autobiographies of these senior members of the Association show that all of them had for a foundation general training in hospitals even when internships were not required for state licensure. All had expected to practice general medicine and surgery. Because little was known about otolaryngology and its interrelation to general medicne and surgery, it was not considered to be a suitable career for well-trained doctors. However, it was observed gradually that the diseases and lesions affecting the anatomic field of the ears, nose, pharynx and larynx were of great importance to the physical well-being of patients. This attracted the attention of these serious minded, well-trained physicians who thereupon decided to learn more

about this special field of medicine. As their knowledge of and enthusiasm for the specialty increased their services became sought for as teachers.

Teachers are born and not made. They comprise the qualifications of a certain type of individual person. Of teachers there are those who are loved and respected because of a certain kindliness and helpfulness that inspires students. There are those rigid individualists who, because of their deep interest and enthusiasm, have great ability to teach but in doing so become strict disciplinarians and drivers. These men are more respected and revered in after years than during the training period. There are teachers who have the ability to inspire by example certain types of young men to become interested in much needed research as it applies to the special field. Always, and fortunately for medicine, there will be those physicians who are not satisfied with superficial knowledge of clinical phenomena but for their own satisfaction require to learn the more underlying reasons for the occurrence of baffling clinical syndromes. The information gained is then passed on to the profession for the benefit of patients. This Association of physicians has had the foresight to accumulate a fund for fostering and encouraging research pertaining to their special field. Physicians not members of this Association are eligible to the benefit of that fund.

In the past during the formative period of the study of otolaryngology, attention was directed to clinical, anatomic and pathologic investigation. Curiously enough physiologic aspects of otolaryngology were not developed until fairly recently. The demonstrations of gross and histopathologic specimens, anatomic dissection and surgical technics have always been more spectacular than the demonstration or description of physiologic phenomena. However, it has been observed frequently that many distressing clinical syndromes can be explained best on the basis of altered physiologic reaction because actually no definite pathologic change can be observed or demonstrated. Patients want to be relieved of symptoms and are not impressed unless a rational explanation is given and symptomatic relief based on it secured.

Doctors Packard and Coates began the study of otolaryngology by virtue of a fortuitous opportunity in Philadelphia. Both had prepared for careers in general practice and surgery. Doctor Mosher

became interested in otolaryngology while establishing a practice in general surgery. Doctors Wood and Barnes did not mention the circumstances surrounding their adoption of otolaryngology. Doctor Shurly entered special practice under the sponsorship of his uncle, a distinguished practitioner in Detroit.

Preparation for the work in what is now the field of otolaryngology was obtained in different ways. Doctors Mosher and Wood began their fundamental training in Germany in the clinics that were organized for that purpose. Doctor Mosher became interested in the anatomic aspects of the field and decided to develop a teaching center in Boston. In this wish he has succeeded until at the present time his center stands second to none in the world. It followed quite naturally that because of his knowledge of anatomy he devised and developed surgical technics which remain rational and effective when properly applied. Influenced by Killian he became interested in bronchoscopy and esophagoscopy and has contributed much to these fields. Apparently he had much native mechanical ability if the instruments he has devised are an index. His ability in illustration, although a disappointment to him as a possibility as a career, has added to the clarity of his word descriptions. That he has succeeded as a teacher is evident by his greatest monuments, the men he has developed. These men have become leaders in the specialty. No teacher should ask for greater honor. Other accomplishments of Doctor Mosher are the great influence he has had in raising the general standards of practice through his publications, his critical discussions at medical meetings and his insistence on high standards for certificates by the American Board of Otolaryngology.

Doctors Wood and Barnes placed pathologic significance of lesions on a high plane in the specialty, especially in relation to rational bases for the removal of infected tonsillar tissue. At the turn of the century and for two decades following there occurred what has been called the era of "massacre of the tonsil." It was the influence of the pathologic studies of these observers that gradually produced a change in attitude. The theory of the focal infection cause of certain syndromes was the rage in the second decade and there is no doubt many tonsils were removed for inadequate reasons. The function of the tonsillar tissue still is a moot question. Doctor Wood confirmed Goodale's findings in acute tonsillitis which were that infecting organisms gained access to the tonsillar parenchyma

only if there were present ulceration of the crypt epithelium. Doctor Barnes became interested in the treatment of inoperable malignancies of the paranasal sinuses and paved the way for the present accepted methods of treatment.

Doctor Packard besides what he has contributed to otolaryngology, activated by the inspiration of Sir William Osler, has become known for his erudite historical studies and publications. To have a member of the Association known as an outstanding medical historian reflects great honor on the Association.

Doctor Shurly was probably one of the first to observe the effect of what are now known as vitamins on the well-being of sick patients.

Doctor Coates will always be known for his teaching and clinical acumen. His kindliness and helpfulness has inspired his students, now his monuments, to carry on. His publications have been authentic and his textbook has filled a great need. He overcame his natural diffidence by persistence. His influence is felt whenever otolaryngology is discussed. One of his greatest contributions for the good of the specialty is the encouragement he has given to younger men.

It was found difficult to express adequately what should have been said in eulogy of the distinguished senior members of the Association, but be it known to them that we, the membership, are deeply grateful for their outstanding contributions made under such difficulties and for their inspiration and guidance. We have profited by their example and it is our hope that we too may be held in the high esteem of the membership as we also attain the level of senior membership.

A FORMER SECRETARY'S APPRAISAL OF EARLIER PROGRAMS OF THE ASSOCIATION

GEORGE M. COATES, M.D.

PHILADELPHIA, PA.

Dr. Hill has asked me to go over the records of the Association from the meeting of 1921, when I first became Secretary, until 1933, in order to analyze the programs from an historical point of view, and to comment upon some of those forgotten worthies who made medical history therein.

In some ways this is a pleasant task, but since I also for some time held the office of Biographer and Historian it was my sad duty to prepare memorials for many of our departed Fellows.

In taking up the Transactions of the Forty-third Annual Meeting, held at the Old Chelsea Hotel in Atlantic City in 1921, I was shocked to discover that of the sixty-two Fellows registered there are only fifteen survivors, and the figures for the succeeding meeting were almost identical; i.e. 61 and 14. There were seventeen papers presented, the authors of only five of which are still with us; and of the officers, only Dr. Mosher and myself; and of the Council, Drs. Goodale and Halsted. No wonder the younger members of this group know so little about their predecessors, as was disclosed in President Hill's recent questionnaire.

However, Tempus Fugit, as Ross Skillern entitled his Triological Society presidential address. The programs of those days in the twenties were constructed around the wishes of the incoming president, who usually suggested a symposium of three or four speakers. The remainder of the program came from volunteered papers, about a dozen, which were grouped by the secretary according to similarity of subject. There was never any dearth of offerings. For instance, in 1921, with Dr. Mosher in the chair, the symposium was on laryngeal tuberculosis. Two Trudeau guests, Lawreson Brown and Carroll Edson spoke on general measures of treatment and the influence of climate, while Robert Levy of Denver discussed surgery,

and Lee W. Dean took up treatment by suspension laryngoscopy. Levy had spent his professional lifetime treating laryngeal tuberculosis, while Dean, then dean of the School of Medicine in Iowa State University and director of the Department of Otolaryngology, was a pioneer in many branches of our specialty, notably the early diagnosis of sinus infection in young children in relation to arthritis, and the influence of middle ear and mastoid infection on the gastro-intestinal syndrome—then currently called cholera infantum, athrepsia, malnutrition, etc. Suspension laryngoscopy, introduced by Killian, had been improved by Robert Clyde Lynch of New Orleans. Other papers on this notable program were mostly on advanced subjects of discussion in the medical world. The tonsil question in the twenties was not entirely solved, and subject to debate as shown by Tonsillectomies in Adults for Rheumatism by Hill Hastings of Los Angeles, Results of X-ray and Radium Treatment of Tonsils and Adenoids by D. Bryson Delavan of New York, and Must It Always Be Tonsillectomy? by Henry L. Swain, Professor of Otolaryngology at Yale. Delavan was the Nestor of the Association, had almost been one of our founders, was a contemporary and student of Morrell Mackenzie in London, and the second Secretary and fifteenth President. He was later, in 1939, elected to a second Presidency on the occasion of our Fiftieth Anniversary. Swain's paper was partly in defence of the original tonsil operation, tonsillotomy, then nearing oblivion.

Ventriculo-chordectomy was presented by Chevalier Jackson, who had moved from Pittsburgh, the scene of his early fame, to accept the Chair of Laryngology at Jefferson Medical School in Philadelphia. This operation, with the imposing but self-explanatory name, was probably the first successful attempt to restore the airway in cases of obstruction due to abducens paralysis, and it was the forerunner of the several present-day procedures to open the glottis permanently, thus doing away with the tracheotomy tube. Papillomas of the Larynx was discussed by O. A. M. McKimmie of Washington, D. C., and then the program continued with Diseases of the Accessory Sinuses, then rapidly becoming of primary interest after years of minor neglect. Mucocele Treated by Surgery was described by Virginius Dabney, also of Washington; Aspergillosis of the Maxillary Sinus by Ross Hall Skillern of Philadelphia; and Intranasal Ethmoid Exenteration with Hemorrhage and Death by Dunbar Roy of Atlanta, Georgia, later to be the president, and who was

also an ophthalmologist of repute. Skillern had studied in Vienna with Häjek, and some time after his return brought out his book on the nasal accessory sinuses, which was to run through five editions. One of Häjek's students asked him what he thought of Skillern's book. "Well," said Häjek, "Skillern asked me if he could translate my book, and I said 'No.' Well, he did it anyhow."

Neuralgia of the Trigeminal Tract, by Charles H. Frazier of Philadelphia, an eminent neurosurgeon; Nasal Tuberculosis by William B. Chamberlin, professor at Western Reserve; Pulmonary Suppuration Treated by Endobronchial Irrigation, by Charles J. Imperatori of New York; and Group Head Surgery, the result of his military experience in World War I, by Burt R. Shurly— all of these three later to hold the office of president. Radium Emanations, a new subject then in Laryngology, was presented by Otto T. Freer of Chicago, the designer of many special surgical instruments still in use today, notably those for the submucous resection of the septum.

Another group of papers consisted in The Use of Radium in Carcinoma of the Larynx and Esophagosus, by Crosby Greene, Jr. of Boston, John R. Winslow of Baltimore and Fielding O. Lewis of Philadelphia. This group, as well as the earlier one mentioned above, emphasized the study and importance of the comparatively new radio-active substances, which study is going on actively unto the present time. Crosby Greene contributed brilliantly to the work of the Association, cut short by his untimely death. Possessed of a fine baritone voice, he lead the "choir" at Triological dinners, in which he was joined, among others, by Burt Shurly, Ross Skillern and Bill Chamberlin, all standbys for years. His solos were always in demand at our banquets, and especially his "Here's a Health to Prince Charles." Another prima donna was Norval Pierce of Chicago, and it was his "Mandalay" that enthralled us. He had been an opera singer before studying medicine, and his great interest was in the larynx. His literary contributions were of value. . . . Finally, the presidential address by Mosher on Cardiospasm was a Continuation and development of his long-standing investigation of the anatomy concerning the esophagus and its surrounding parts, a study that has become a classic in our literature.

So much for the papers and the personalities of the men who wrote them. What deductions can we draw from them? In the

first place, the authors were unquestionably among the leaders of national and international thought and progress on laryngological subjects, a position which has been amply maintained, as it was in the forty-five previous meetings, down through the succeeding years to the present time. In the second place, a study of the published transactions will show the scope of the discussions of these subjects, which were often of equal value with the papers themselves. None of the discussions were formally "opened" on the program—they were spontaneous, free and frank. A good paper, and sometimes a poor one, should draw discussion, thereby amplifying the subject, injecting different personal views, correcting unsound deductions, as well as backing up, with personal experiences and case histories, the stand taken by the author. And finally, such a survey shows that the Fellows of this Association were no old fogies, repeating the theories and mistakes of the past, but up-and-coming students and investigators of the constantly appearing new surgical methods, diagnoses and therapy engaging the curiosity and attention of the time. This has been called an old man's society, because a man must be matured, have established a reputation and produced sufficient literature by which his accomplishments and eligibility may be judged before his admission to fellowship. The constantly diminishing number of Fellows in the higher age brackets, and their replacement by younger, coming men, assures that we will never be a society of has beens or dodos.

I have described the 1921 program at some length, since it is typical of subsequent meetings of the Association. Time, of course, prevents close analysis of those following, in the production of which I was concerned by reason of my position as Secretary. So many recollections come to one on reading over the volumes of Transactions produced during those years that it is somewhat difficult to pick out the highlights, and an old man's ramblings, however interesting to himself, may bore others when they concern those whose accomplishments, and even names, have passed into oblivion. This is bound to happen to most of us, in the not too distant future, and to all of us in time.

Harmon Smith of New York, for seven years Secretary, was the forty-fourth President. Papers on bronchoscopy by Thomas Hubbard of Toledo, on the sinuses by Cornelius G. Coakley of New York, Skillern, and Rockwell A. Coffin of Boston continued the

trend of the previous meeting. Now allergy was introduced for the first time by Joseph L. Goodale of Boston and some invited guests, and the tonsil question was continued by George B. Wood of Philadelphia and Charles W. Richardson of Washington, D. C. Five papers on laryngeal carcinoma were given by Waichero Okodo of Japan, Chevalier Jackson, Herbert S. Birkett of Montreal, John E. Mackenty of New York and Otto T. Freer of Chicago. Greenfield Sluder of St. Louis introduced his work on spheno-palatine ganglion in two papers, which culminated in his extensive and thought-provoking book on Lower Half Headache, while Thomas R. French, a veteran from Brooklyn, described the tongue, especially the lingual tonsil and infratonsillar lymph nodes as a source of systemic infection. Of these authors Coakley, French, Birkett, Hubbard and Goodale were past presidents, while Wood, Richardson, Jackson and Sluder were destined for that honor.

After years of usefulness, Hubbard, on account of infirmities, took to word carving, and his beautiful work was accounted for by the skill developed in his surgical and bronchoscopic training. Coakley was a veteran teacher and a leader, whose opinions carried great weight either in debate on the floor or in the Council. Rockwell Coffin and Joseph Goodale were (and in the case of the latter still is) thoughtful students and researchers in new developments in our specialty, and in the case of Goodale, it was he who, as the first laryngologist to seriously take up the study of allergy, really gave it a place in our special field—a work so ably carried on by French K. Hansel of St. Louis. Wood was known for his profound studies on the pathology of the tonsils and their lymphatic drainage, and Richardson — Uncle Charlie to many of his younger associates— entertained lavishly when the Association met every third year at the Raleigh Hotel in Washington, which it was compelled to do by its connection with the late unlamented Association of American Physicians and Surgeons. On the other day of the session, Dr. Joseph H. Bryan gave a delicious luncheon for the Fellows, and there was much rivalry between these two Washingtonians, not only in entertaining but in other matters as well. Mackenty did tremendously important work in improving laryngectomy to the point where it no longer had a major mortality rate, and his work was outstanding inthe world, as was his work on cleft palates. He was a radical, spurning thyrotomy in spite of the brilliant results of St. Clair Thomson and others. If cancer, even of only one cord, was

positively identified, he felt that total removal of the larynx was the safest procedure, and feeling thus he lent his great influence to the development of the artificial larynx first, and later the esophageal voice. A big man with a hasty disposition and a large vocabulary of unconventional words, he, as first vice-president, was called on to preside at the meeting in Montreal when Sluder was taken ill en route. Sluder's very learned and abstruse manuscript was given him to read, but after trying several pages he refused, saying he could neither understand it nor pronounce the words. It then became my job to attempt it, though I was as much at sea as Mackenty. I'm sure that, as it was read without understanding and with stumbling over unfamiliar words, the audience breathed a sigh of relief when the performance was finished. Incidentally, Mackenty adjourned the meeting half a day ahead of schedule in order to hurry back to New York.

Subsequent programs of the Association emphasized many phases of the subjects outlined above, and with new faces and voices constantly replacing the old. In 1923 Emil Mayer of New York was President—another "Uncle," this time Emil, to his younger admirers. Both Uncle Charlie Richardson and Uncle Emil Mayer addressed their following as "dear nephews," and gloried in the affection implied in their assumed relationship. Mayer had a fine, broad understanding of all aspects of laryngology, and his work on the question of local anesthesia and its hazards, done as Chairman of a Committee of the American Medical Association, was outstanding, and contributed much to the stabilization of a subject until that time not too well understood. Mosher and Mackenty continued their comments on the topics of recent previous years, and a newcomer, Ross Faulkner of New York, became one of the sinus enthusiasts who, with Skillern, were in favor of more extensive, or even radical, surgery. Francis P. Emerson of Boston, although usually considered more of an otologist, contributed to our Transactions valuable data on the influence of chronic upper respiratory tract infection in relation to general disease. H. I. Lillie, who has been a consistent producer, made his first appearance on our programs in 1923, but he needs no introduction to any of us, nor does Francis W. White of New York. Joseph B. Greene of Asheville, however, may not be remembered or known to our younger group. His contributions were mostly on laryngeal tuberculosis in its many different aspects, and his investigations in regard to postoperative tonsillar hemor-

rhage. Gordon Berry of Worcester, Massachusetts, came into the picture in 1923—and in many subsequent meetings. He was to become Acting President on the death of George Fetterolf, and later, as you all will remember, President in his own right. Perry Goldsmith of Toronto is also still with us, and therefore needs no further mention, except to say that he was for years Professor of Otolaryngology in the University of Toronto and a notable contributor of discussions of conservative laryngology. Samuel McCullagh, aside from his contributions on ethmoiditis, especially as to the efficacy of radium in the treatment of nasal polyposis, also presented esophageal malignancies. He was Surgeon-Director of the Manhattan Eye, Ear and Throat Hospital. At the Annual Banquet in 1923, President Emil Mayer introduced an innovation of having each of the newly-elected Fellows make a speech. Raymond McKinney of Memphis, Professor in the University of Tennessee, electrified the banqueters by satirizing the older Fellows, with somewhat less than wild applause, and in consequence was in the dog house for some years. Mayer also presented an aquacade in the tank of the Ambassador Hotel—a form of entertainment much more appreciated.

Programs of the next few years followed the same general pattern, with old actors and new appearing on the scene. Carcinoma of the esophagus, larynx, trachea and bronchi continued to receive great attention, both surgical and radiological treatment being considered, by Crosby Greene, Jackson, Henry Hall Forbes of New York and Mackenty, while stenosis of the larynx and trachea was considered by McKinney, Imperatori, Clement F. Theisen of Albany and Frank L. Dennis of Colorado Springs, calling attention to lye strictures and the great work of Chevalier Jackson in having legislation passed in eventually all states compelling the branding of lye preparations as dangerous. Laryngeal tuberculosis continued to hold attention, discussed by Frank R. Spencer of Boulder, Colorado, who wrote often on this and allied subjects, and who was one of our recent presidents. There were several papers on papillomas of the larynx by Hubbard and McKinney, and then a number of subjects that had not appeared previously—i.e. syndrome of Avellis by Imperatori, status lymphaticus by James A. Babbitt of Philadelphia, carcinoma of the trachea by Thomas J. Harris of New York, a tonsil paper by Secord H. Large of Cleveland, diagnostic problems by William V. Mullin, then of Colorado Springs and later of the Cleve-

land Clinic, nasopharyngeal fibromas by Gordon New and osteomyelitis of the cranial bones by Harold I. Lillie, known then as now to his friends as "Pete." Frank Dennis was a brilliant investigator, with Bill Mullin, on the lymphatic drainage from the head. Mullin was Secretary, with his promising career cut short by his untimely death from cavernous sinus thrombosis. Jim Babitt is, I am sure, well remembered not only for his great professional writings but also for his genial and friendly disposition. At a meeting of the Council in Imperatori's office at the outbreak of war, he was asked, most unexpectedly, to offer a prayer; it was given spontaneously and was most beautiful and thrilling.

Tommy Harris had been for years Secretary of the Triological Society, then its President, then Secretary of the American Otological, its President, and again its Secretary, and was Director of the Army course in otolaryngology at Fort Oglethorpe, Georgia, during World War I, where our present President served as his righthand man and where good work was done. Gordon New made his first appearance before this group in 1924, and again in 1925 on pemphigus, and Arthur Proetz gave the first of his many and invaluable studies on nasal physiology—this time olfactometry. Other new subjects in 1925 were plexiform neuroma of the larynx by Forbes, rhinoscleroma by Wood, and speech correction by Max A. Goldstein of St. Louis, who will be long remembered for his work in speech training and correction in the deafened, and for his founding and organization of a very wonderful institution, the Central Institute for the Deaf.

Pachydermia laryngis by Lewis (F. O.), lung abscess following tonsillectomy by Edwin McGinnis of Chicago, and the use of vaccines in sinus disease by Ralph A. Fenton serve to show the variety of subjects discussed. Of the authors just mentioned Hubbard, Babbitt, Imperatori, Jackson, Spencer, Proetz, Wood and Lillie have been our presiding officers.

In subsequent years the sinuses continued to attract investigators and writers, such as New, Lee M. Hurd of New York, and Leon E. White of Boston, whose great contribution was the connection between sinus infection, or negative pressure in the sinuses of the posterior group on the optic nerve, and the production of retrobulbar neuritis. His studies were epochal and the subject new to our Transactions. Gabriel Tucker of Philadelphia appeared in

1926 with his work on laryngeal stenosis following tracheotomy, and George E. Shambaugh, Sr., decried many of what he called fads and fancies, such as that sinus disease causes headache, that a submucous resection of the nasal septum often produces the relief for which it was done, that tonsil surgery was frequently unnecessary, ethmoid and maxillary sinus surgery for headache when the cause was elsewhere and not carefully looked for and many other procedures. Shambaugh was known principally for his otological studies and contributions, especially on the anatomy and physiology of the internal ear.

Thomas E. Carmody of Denver, later President, always presented valuable papers and forceful discussions, particularly on subjects relating to the mouth and sinuses, since he was also a well-trained oral surgeon, as well as a rhinologist. One of the founders of the American Board of Otolaryngology, he often confounded a candidate before him for examination by asking the order of eruption of the teeth and similar questions. Edward Cecil Sewell of San Francisco, introduced at our meeting his external fronto-ethmo-sphenoid operation under local anesthesia, which many critics said could not be done until they had seen Sewell execute it with consumate skill. Ill health compelled his retirement at an early age. It was in 1926 that a paper by Proetz introduced his famous method of displacement irrigation of the sinuses, which revolutionized many standard office procedures. H. Marshall Taylor of Jacksonville, Florida, gave us our first authoritative discussion of the causes of sinusitis, as well as middle ear disease, due to swimming. His work is a classic, dealing with comparative anatomy, the inadaptability of man to an aquatic element, the influence of chilling, and many other factors. Taylor also made great contributions to our knowledge of congenital deafness, showing that the administration of quinine in large doses to the expectant mother might, in susceptible individuals, cause deafness in the child.

Chevalier Jackson was President in 1927, and of course his presidential address was concerned with peroral endoscopy, especially in regard to teaching the subject. In his program a symposium on lung abscess consisted of five papers, three by guests and two by our Fellows—Bryan and Tucker. L. W. Dean produced a somewhat startling paper on sinusitis in infants and young children, and its influence upon their general system, resulting, among other things,

in the production of arthritis. He described in detail his method of diagnosis by obtaining uncontaminated cultures from the maxillary sinus, and his method of treatment which varied from diet and climate changes to tonsillo-adenoidectomy to sinus irrigation, and, in certain instances, radical sinus surgery. Laryngeal malignancies continued to hold the spotlight, the emphasis now being on irradiation by Louis H. Clerf of Philadelphia, our present Secretary, who warned concerning possible complications, then not too well understood, and Georges Portmann of Bordeaux, France, a Corresponding Fellow, who preferred to irradiate through a surgically performed window in the thyroid cartilage. It was Portmann, incidentally, who described drainage of the saccus lymphaticus for the relief of Ménière's syndrome. Harry A. Barnes of Boston read a paper on one of his two favorite topics, on which he was an authority, malignant tumors of the sinuses with a widely maintained, semi-permanent opening in the face for direct (and immediate) irradiation and subsequent inspection. His other topic was the tonsils and tonsil operation.

And now our chronology brings us to the Semi-Centennial Meeting with our Nestor, David (seldom used) Bryson Delavan in the chair for the second time, the only repeater in our history. Delavan had been in London with Morrell Mackenzie when adenoidectomy was introduced, and he brought the operation and instruments to America with him, performed the first operations and taught the procedure. He made early studies of cases of nasofibroma, and many different measures for its eradication and control, and continued his studies and writing to an advanced age. A life-long interest was the control of cancer, and he worked indefatigably with the American Cancer Society. Our Guest of Honor was Sir St. Clair Thomson of London, who had visited us before, was our Honorary Fellow, and extremely popular with all of us. Who of us who knew him forget the quotations from Shakespeare with which he interlarded every discussion, always most appropriately? He carried a selected list of these in a little black notebook, which he always consulted in advance of speaking, in order to select the most appropriate one. His great friend and colleague, Herbert Tilley, carried a similar notebook filled with anecdotes and stories which he used successfully in the same manner. Thomson's home in London was destroyed during the Battle of Britain, and he retired to his native Edinburgh, as he told me, an old and broken man seeking

to live out his few remaining years in quiet. He was shortly knocked down in the street and killed by a motorcyclist.

Dr. Delavan took great pains to make the fiftieth meeting a memorable one. Through the cooperation of V. Mueller and Company, well-known instrument makers of Chicago, an exhibit was arranged to include examples of all known laryngeal instruments from 1872 onward, a truly amazing collection, which is listed in the Transactions of that year. The instruments on exhibition totalled 501. The program was shortened from the usual fifteen papers to twelve, as one half-day of the usual two and a half day session had to be reserved for the Congress of American Physicians and Surgeons, in which, in common with all of the national special societies, we held membership. This Congress never proved popular or was well attended, and after languishing for a few more years, was finally dissolved, to the great relief of everyone except the Congress officers. At a general meeting of the Congress Dr. Delavan delivered a superb address on the History of Laryngology, which, with photographs of all the pioneers, is to be found in the 1928 volume of Transactions. The attendance, however, was shockingly small, so few from other societies attending that our Council took measures, with several of the other oragnizations, to discontinue these meetings in the future. The presidential address was also an historical review of the American Laryngological Association, and should be read by every incoming new Fellow. The Guest of Honor, Sir St. Clair Thomson, contributed an essay on laryngofissure for intrinsic cancer of the larynx, the procedure for which he was famous, and with which he had had great success in reducing the mortality from this disease. William V. Mullin, now of the Cleveland Clinic, at that time soon to become Secretary, read a paper on the relation of the thyroid to the larynx, and there were two other papers on the surgery of laryngeal carcinoma by Mackenty and New, the latter taking up the cudgels for a two-stage operation. Colonel Harris P. Masher looked backward on American otolaryngology in the World War (I), summarizing the accomplishments of our branch of medicine and pointing out deficiencies and faults, mostly of supply and organization beyond our control, to be avoided in the future. One great accomplishment that bore fruit in Army organization for and in World War II was the recognition of the specialist in medical team work. Gordon Berry spoke on dental caries in relation to sinus infection, and Sewall continued his im-

provements on the external fronto-ethmo-sphenoid operation. The bane of all frontal sinus surgery of the radical type had been the closing up of the nasofrontal duct, and Sewall proposed to correct this with an osteoplastic flap. Theisen's topic was ethmoiditis in infants and young children with orbital complications, and Dabney's, osteomyelitis of the frontal bone. Larsell and Fenton received the Casselberry award for their study of otalgia and the sphenopalatine ganglion connections.

The fiftieth banquet was a gala affair, more largely attended than any previous dinner. The punch (remember it was in prohibition days) was procured, concocted and served, if my memory fails me not, by Hal Tobey and Ted Porter, and proved most popular. At one stage of the dinner, I noticed that Dr. Delavan, a meticulously correct gentleman of the old school, seated at the head table with Dr. Thomson on his right, was looking very distressed. There was considerable noise at the tables and some not too melodious singing. I went to the President and asked him if everything was all right. He replied, "Not at all. This uproar and noise is disgraceful. What will Sir St. Clair think of us?" Since Sir St. Clair had been our guest before and was a thoroughly good sport, I was not worried on that score. I was sure he was enjoying himself and only wished he could be down on the floor to join in the singing. However, I said to Dr. Delavan, "Would you like me to speak to them?" He replied emphatically, "Yes, if you please," so I went to each noisy table and gave them the message, whereupon all tumult immediately ceased, and the rest of the evening was passed in perfect decorum. The next morning at breakfast I asked Dr. Delavan what he thought of the banquet, expecting some criticism. "Why," he replied, "I think it went off very well indeed." "It was a little noisy, perhaps," I suggested. "Do you think so?" said he, "I thought it was very quiet, orderly and respectable; quite in keeping with the dignified tradition of our great Association."

So ends my attempt to comply with Dr. Hill's assignment. Time flies, and those of you who are still young, at least in the estimation of this older men's society, will soon be the oldsters, and we who are now of the older group will have passed on and soon be forgotten except as names of a past medical generation, always excepting those few immortals whose works will always be remembered. Those whom I have mentioned, and many, many others,

have made medical history as teachers, investigators, writers and clinicians. Our Association has stood, as it still stands, in the very first rank, as the first national laryngological society in the world, and a more careful survey of our programs, from the first in 1879 to the present one, amply sustains our position of preëminence in the laryngological world. I have no fear that the oncoming generations of Fellows will fail to keep up the record, and, in time, surpass it.

When a man gets along in years he tends to look back on the great men of the past, and to measure them against the greats of today. Those that I have mentioned so briefly were great men, working with the knowledge of their times and contributing to the advancement of medicine. They compare favorably with their successors who have carried on from where they left off, and who, without the foundation laid down by them, would not have advanced to our present state of knowledge. If those who have gone on were alive and working today, they would still be in the front rank. Time moves swiftly, and men and their works are soon forgotten, the memory of them submerged by the newer medicine and the men who are making it so successfully. They, in their turn, will share the same fate, but let us not entirely forget those who have gone before; let us remember some of their contributions that have helped make our present medicine what it is, and preserve their names for a little while longer from the oblivion that surely and swiftly eventually awaits all of us.

RECENT ADVANCES IN OUR KNOWLEDGE OF CANCER

JOSEPH C. AUB, M.D. (By Invitation)

BOSTON, MASS.

When your President asked me to talk about this subject I was puzzled as to what you would like to know about a field in which the great discovery has not been made. It is easy enough to talk about a problem in which the great discovery has been made but the great discovery of what constitutes cancer is still not known.

In thinking this over, I decided to divide my few minutes in three parts: first of all, a few words about diagnosis; secondly, a few words about treatment, and thirdly, the question of understanding of the disease, if there is time.

First of all, about recent advances in diagnosis, I think the most interesting one is that of the Papanicolaou stain. It is being used more and more in the clinic. Forgive me, but of course I am as much clinician as I enjoy the laboratory. The Papanicolaou stain test has interested me very much because it is very much better than I thought it would be in diagnosis of tumors. It is applied to nearly all secretions, as you all know but so far I have not heard of a report of its being used in the nasopharynx. I think this problem ought to be thoroughly investigated. You all know about the Papanicolaou stain and I need not discuss it. It has from my point of view one very interesting factor, that is, that it is dependent upon the fact that tumors slough off apparently viable cells, and it is these viable cells—they look viable at any rate—on which the diagnosis rests. Normal tissue like mucous membranes also slough off cells but they are the old cells and whether they are viable or not is questionable. I doubt that they are, though I have no evidence for that. Neoplasms slough off cells very much more readily than do normal tissues and it is these sloughed off cells that are used in the Papanicolaou stain to make a diagnosis. The reason why they do this, I think, is explained by some work of Coleman of Philadelphia, who showed by some very pretty experiments that neoplastic cells have much less cohesiveness than have normal cells. Coleman has taken a micro dissector, put it under the microscope and has pulled the cells

apart. He pulls the cells apart by putting stress on contiguous cells. It takes much more stress to separate normal tissue than it does tumor tissue. There is obviously a change in the cellular phase of the tumor cell which makes them much less cohesive than is true in normal cells. This indicates an important difference in tumor cells and implies handling of neoplasms because if one does like surgeons have done for years, remove a tumor without paying attention to the possibility that he may be sloughing off cells, he can be seeding his tissue operative field, whereas a normal cell might not be so sloughed off.

Some method, it seems to be evident, needs devising on the basis of this work by which one covers the surface of a neoplasm so that these easily sloughed off cells are not seeded in an operative field to produce the metastases which one wants so hard to avoid. I realize that in the naked pharynx this is particularly difficult, but each incision through a neoplastic field may spread and of course, as you all know, it is this first attack in surgery, the first attempt to remove a tumor which is your really only possible chance of curing a neoplasm. Therefore, it must be radical and in some way or other surgeons must learn either by coating the surface of a neoplasm some way, or by carefully guarding it, that one does not disperse neoplastic cells which lack cohesiveness, in the field in which they are working. Later attempts after the first surgical procedure slow up the disease but rarely cure it. The first attack on tumors has to be radical. You must not seed the area with these easily dispersed cells. Somehow or other one has to learn how to do that. Someone will find a way of coating tumors so that these cells cannot be dispersed. So far as I know that has not been done. It would be a most interesting way of attacking the problem.

The second interesting problem in relation to practical work in tumors is with radioactive isotopes. I am only going to say a word about it because I don't think it offers much opportunity or advantage in laryngology. Radioactive isotopes could be a wonderful way of diagnosis in tumors if one could localize them in the tumor itself. If somehow or other a compound could be put into a tumor and in larger concentration than is found in normal tissues—and I made an attempt at that some years ago with dyes, because dyes are supposed to go into tumor tissue more specifically than in other tissue—that would be fine. These dyes do go into tumors a little

more than they do in normal tissue but the concentration is not sufficiently differential to warrant their use in the diagnosis of tumor. It is only in two tumors that radioactive isotopes have so far been proved to be of good diagnostic value. One of them of course is radioactive iodine. That can be made easily and it has the characteristic of going specifically, almost preferentially, because it goes to the pituitary and a few other tissues, into thyroid gland and one can tell by the amount that goes into the thyroid tissue whether the thyroid tissue is overactive or normal. In a few cancers of the thyroid it is also concentrated in the malignant tissue, not in all of them, because some tissues as they become malignant have lost their function and lost their function and lose their ability to concentrate iodine. But, on the whole, the use of radioactive iodine is the characteristic material to use in such tissue and to localize the radioactive isotopes in these tissues it is a simple matter to put a Geiger counter in the area. Once one puts in the radioactive iodine all one has to do is to put a guard or screen the individual and one can find where the greatest contraction is by means of this Geiger counter.

The only value for diagnosis is for tumors of the brain where Selverstone and Sweet have shown that radioactive phosphorus is localized in tumor itself. That is of great importance and it is based on the fact that the blood barrier of the brain does not allow inorganic salts to migrate from the blood to brain, whereas the concentration of radioactive phosphorus in tumors of the brain is a little higher than in normal tissues, but not as high as in the liver, but the fact that there is a little radioactive phosphorus in tissue and considerable in the tumors of the brain allows the brain surgeon to localize tumors in a rather dramatic way by means of a small counter which he can insert in the tissue and can show by the speed at which the counter is counting where the malignancy is.

As far as the nasopharynx is concerned, there is very little hope so far for using that as a diagnostic procedure to show where the tumor lies for the reason that the differential accumulation of anything we have as yet is not great to allow you to differentiate between normal and malignant tissue in an area composed of the type of cells that are present in the nasopharynx. So much for diagnostic tests.

Now as to newer methods of therapy, surgery and x-ray remain the treatment of choice for all neoplasia. They are getting progres-

sively better. There is nothing new which compares with complete eradication of a tumor by surgery. There is nothing new which is very much better in radiation than x-ray, so I start right off by saying the time honored methods of treatment remain, surgery and x-ray. But several attempts in the last few years have been made to specifically kill tumor cells. None of them have been specific enough to be of great value.

If I may just summarize our experience with them, the nitrogen mustards are of value in lymphoid tissue and are of value in some tumors of the lung, particularly oat cell tumors. They injure the dividing cell just the same way x-ray does and therefore they hit the cells which divide most rapidly. The cells which divide most rapidly in the body are the white cells of the blood stream. Polymorphonuclears live four days in the blood stream. The platelets live about that amount, maybe a little less. Lymphoid tissue according to Flory lives about eight hours and lymphocytes, according to Flory, are replaced about three times a day. In tissue cultures I will admit lymphoid tissue lasts longer than that but in the body according to Flory's work, which I thought was pretty, the lymphocytes last only eight hours of the day. Now you can see why Hodgkin's and the other lymphocytic neoplasia fall into the same category that happens to lymphocytes.

If one has a substance which injures cells which are dividing, one would expect and one finds that the blood cells are injured proportionately practically to the malignant lymphoid tissue of the Hodgkin's disease and other related cells. Therefore, the nitrogen mustards, though they produce dramatic effects on lymphocytic neoplasia, do it while also causing rather disastrous effects to the white cells in the body and if one gives enough to knock out the Hodgkin's tissue one also tends to knock out the white cells of the blood stream so that you get into difficulty yourself, and one gets down to counts of 250 for white cells. Just before I left the hospital I saw a patient who had mycosis fungoides who had responded brilliantly to mustard. This was his fourth series of treatments but his white count had gone down to 750, and he had broken out in the most remarkable purpura and was bleeding from his bladder because his platelets also had disappeared from the blood stream, so we have reached the point where in trying to knock out his mycosis fungoides, we had also knocked out too much of the white cell content. The

white cells and platelets come back after four or five days. Two transfusions usually solve that problem but anything which will not really solve the problem with the white cells if you are going to knock out the white cells completely obviously the person cannot survive. Therefore the chances are that the lymphoid tissue of Hodgkin's disease also survives and eventually comes back. The treatment is very much better in early cases than it is in late ones, and most of our experience has been with late cases which no longer respond to x-ray.

In the few patients we have tried it on before the x-ray, the nitrogen mustard works very much better and the relief from symptoms may go into many months. If one does it late after x-ray treatment has failed, then the improvement by nitrogen mustard is usually a matter of six or eight weeks, whereupon the disease recurs.

The other substance which has been used as a chemical method for improving neoplasia is urethane, a drug which many of us used in physiology as a method of anesthesia. Urethane also has a preferential selection in causing death in dividing cells, and it is particularly of value in some cases of myelogenous leukemia and the leukemic infiltrations that one may find in the body, but urethane, except for that, has offered very little in our hands. It does keep myelogenous leukemia patients well under control and is therefore worth a trial because you can keep it up indefinitely, and in some patients has given us pretty good results.

I am not going to talk about the folic acid derivatives. You have heard so much about them and in our hands they have been very depressing. In other people's hands they have solved problems of leukemias in childhood but with us who are working on adults, we don't seem to find them helpful.

I would like to say in the minutes that remain a few things about and go over rapidly what I think of the neoplastic problem. One can only theorize about what constitutes neoplasm. We don't know the difference between normal cells and tumor cells. It essentially comes down to one thing, a very simple problem, but it is such a fundamental problem that it is very hard to solve. The one thing is that normal cells stop dividing and what is more important, normal cells stop dividing when they come back to their normal number of cells; no matter what you do, normal cells stop dividing. If you take out two-thirds of the liver in a rat, in two

weeks the number of cells has returned to normal and cell division ceases. Neoplastic cells don't stop dividing, and that in a very simple way, is what constitutes the problem of neoplasm. It is such a fundamental problem because cell division is, after all, the whole basis of life that it is proving a problem very hard to solve.

The rate of cell division in normal tissue and in neoplastic tissue is about the same. Neoplastic cells divide about once in 46 hours. In our normal rat livers which we have depleted where regeneration recurs as rapidly as possible, cell division occurs once in 48 hours. It is approximately the same.

The fibroblasts in tissue culture do almost the same thing. Nearls tissue culture, wherein you put one fibroblast, divides at a great rate and one cell becomes 110 cells in ten days, a little bit faster than it is in the body, not very different. It comes out about the same. So tumor cells don't divide more rapidly than normal but just keep on. In order to acquire that characteristic takes time. No neoplastic cell apparently starts out without a latent period. A latent period seems essential with every one of the carcinogenic materials. With methyl cholanthrene it takes about six weeks. With every one we know of there is a latent period. It does not switch from normal to malignant tisue.

There may be two factors: one, that a malignant cell is formed, and second, you have to have a stimulus to make it divide, to make it progress. There is some evidence for that but we don't know about that. It is one of the great arguments which we always have in our laboratory and it is between Bierenblum and our point of view, that the neoplastic cell is a gradual change. Birenblum did a cell and he said he cannot repeat it. He put on a neoplastic substance, methyl cholanthrene and croton oil. Croton oil does not produce tumors but acts as a stimulant upon division. If you put methyl cholanthrene and croton oil on the skin of mice, he said he gets tumors in six weeks. If he delayed four weeks, eight weeks or twelve weeks, after six weeks approximately after he put on the croton oil, tumors of the skin would appear, implying that by one dose of methyl cholanthrene he had changed those cells to malignant cells and that then a non-specific irritant pushed them on into tumors at the same rate, even twelve weeks after the initial dose. Now we don't agree with that and I am talking too long in getting this far, and therefore I am going to slip over the problem. But

there is much evidence, I think, that there is no sudden shift to neoplasm.

For instance, one can use two or three different methods of producing tumors in animals and they all summate. One can use methyl cholanthrene and a virus, or one can do the pretty experiment of Rouse, methyl cholanthrene on rabbits' ears and going on the way to tumor and then allowing that to subside and the cells return to a condition where you cannot see anything was done to the ear, but if you punch a hole in the rabbit's ear where methyl cholanthrene was applied you get tumors. In the region where the methyl cholanthrene was not put if you punch a hole there you get just normal regeneration. You can do that with butter yellow which produces tumors of the liver. In other words you can use all types of carcinogenic materials and end up in the same way, with the problem of a cell which does not know when to stop dividing. Pre-cancerous lesions also return to normal. You see it in life all the time. You see it in leukoplakia. You have leukoplakia, which is certainly a pre-cancerous lesion, yet properly treated leukoplakia will subside and return to normal. It does not return properly to normal but is much more susceptible to becoming neoplastic later. However, from our point of view there is this gradual shift towards malignancy and then return to normal, which I cannot develop further. Once you get into neoplasm there is much less evidence for that ability to return to normal. Pathologists cannot make the diagnosis very often of neoplasm because many of the daughter cells, according to Wobach, look like adult cells. As you know, the pathologist has great difficulty in making up his mind as to whether a cell is malignant or not but at any rate whether a cell can return from a malignancy to normal tissue we don't know, but we do know that the reverse does take place, that a tissue which is only moderately neoplastic of low malignancy can swing on to much greater malignancy and get progressively more and more severe. Now inasmuch as neoplasia can get more malignant it is obvious that when it first appears it is the one time to eradiate it and not dawdle with the problem.

Can malignant cells become more normal? Can they ever swing from malignancy to normal cells? It is very difficult to find evidence for that. That is one of the problems which has bothered us for many years. Can you get a neoplastic cell and make it return

to normal? That, after all, is the thing which one wants to do which would put all of you surgeons out of business. It would be a nice thing to be able to do. There is some evidence now on which one can work. For instance, there are two tumors which do show regression even though they are very malignant. There is the carcinoma of the prostate, which one certainly can make quiet down by proper use of estrogen and by orchiectomy and now we know that carcinoma of the breast, even with widespread metastases subsides with proper use of things like stilbestrol and testostrone.

As one studies these problems the question arises: do these cells return to normal or what becomes of them? We have been unable to find that these cells change into a normal status. They die. But it is very interesting that even though they die you have the possibility by means of hormones controlling the amount of neoplastic tissue which is present.

What evidence do we have for this? If one takes carcinoma of the prostate with many metastases—they are rare but do occur in lymph nodes—and takes out serial lymph nodes in these patients before you give stilbestrol, before orchiectomy, and follow through, one finds that these lymph nodes disappear because this treatment does control carcinoma of the prostate, but if one takes out these lymph nodes as they are disappearing one does not find normal cells there. One finds necrotic cells, and as the acid prosphatase, which these cell make, diminishes in amount in the blood stream it is associated not with the return to normal of these tissues, but of necrosis of these tumor cells. The same thing was found by Nathanson in our laboratory in relationship to carcinoma of the breast. There one can easily get biopsies and watch these carcinomas of the breast regress with the use of stilbestrol. There too is necrosis of the cell. It is not a return to normal. So we don't have evidence that neoplastic cells can return to normal function, which is what we wanted. But you have evidence that substances like stilbestrol or the estrogens, or orchiectomy are changing your endocrine setup in an individual and so in the body you can control the life of neoplastic cells, and therefore neoplastic cells no longer remain autonomous. You are able to control them and you are able to make them worse. Incidentally, if you give carcinoma of the prostate testosterone, taking a hopeless case who has escaped from all other methods of treatment and you give him testosterone, in five or six hours after you give

testosterone that case will complain of pain in all the metastases in bone, and two or three days later the acid prosphatase which is made by these tumor cells will rise dramatically in the blood stream so by charging your setup of sex hormones in the blood stream one can not only make these cells better but one can make them worse. So you have some control over them, which I think has some comfort. Even though we have not yet learned to change a tumor cell in its one characteristic, to make it stop dividing so that it returns towards a normal tissue, at any rate people who are working in neoplasia are getting a dynamic view towards the problem, a problem which is different from just looking at a pathology and thinking of it as a static process. At any rate we are getting a dynamic point of view of it and trying to influence it physiologically as well as trying to find out what causes it.

DISCUSSION

LEWIS F. MORRISON, M.D.: Mr. Chairman, there are two points in Dr. Aub's address that were very close to home. First, I would like to mention the use of radioactive phosphorus in its application elsewhere than in the brain. Dr. Bertram V. A. Low-Beer at the University of California Hospital has used it in the diagnosis of malignancies of the breast. It has been used also for metastatic nodes in the axilla and in the neck. The results depend entirely on the tissue uptake. That depends upon the increased metabolism of the malignant cells in relation to that of the normal tissue and the mass has to be of fair size before the uptake of the radioactive material will differentiate it from normal tissue. The opportunity to differentiate a small, early neoplasm is not great. The increased metabolism of acute inflammatory areas can cause increased uptake and confuse the findings.

Secondly, it is very nice to have a certain amount of legitimacy added to one's brain child. In regard to the use of the smear technique for neoplasms of the nasopharnx, some three years ago a young Chinese doctor came to the University of California Hospital to study these neoplasms because they are so common in the Chinese. At about the same time tumors of the nasopharynx were brought to the fore at a couple of local meetings. We went through all of the various ways and means of differential diagnosis, how difficult they were to pick up early, etc., and the thought occurred that the smear technique could be used. Since that time—and always when you look for things you usually find them—we have diagnosed 12 neoplasms of the nasopharynx. In the past most of these diagnoses were made from biopsies from nodes in the neck and not primarily from the nasopharynx.

First of all, we had to learn the cytology of the normal secretions of the nasopharynx. In order to keep up the interest factor of those who were really doing the work we selected some visible lesions such as malignancies of the larynx, and hypopharynx, and the tonsil and made direct smears from those lesions as well as biopsies. We had the results from the smear technique that afternoon in certain instances or not later than the next day. Often the biopsy reports were not

available for several days, depending upon how much pressure we put on the Pathology Department.

I want to digress for a moment. Unless there is an exfoliative lesion you are not going to find malignant cells by the smear technique. Those who are interested in the work frequently consider that statement so fundamental that they neglect to mention or emphasize it to people who are not familiar with the method and its results.

There is one other application of the smear technique that has not been popularized. Interesting and valuable slides can be obtained by rubbing the raw surface of a freshly obtained biopsy specimen on a clean glass slide and then treating this slide as one would a routine smear.

I was very pleased to hear Dr. Aub's statement that the method should be applied to the nasopharynx. I am very pleased to report that to date our results have been 100 per cent positive when they should be positive and 100 per cent negative when they should be negative.

NORTON CANFIELD, M.D.: In view of what was said about the desquamation of tumor cells, should we revise our method of tissue biopsy in cases of tumor of the nose and throat?

ANDREW A. EGGSTON, M.D.: Any discussion of malignant cells and the cause of their becoming outlaws always creates a tremendous amount of interest. The study of these cells and what they do and what makes them do what they do always presents a very interesting subject. Progress is being made and with all the money that will be spent in concentrated efforts just as with the atomic bomb, it may lead to an understanding of the physiology of the cancer cell. As Dr. Aub says, when this is done scientists will probably understand the physiology of life.

There are a few things I do want to discuss; for instance, we see multiple malignant disease in individuals. They not only get recurrences of malignancies but also several types and there seems to be a status maligni not unlike a status asthmaticus in allergies. These people apparently are physiologically off balance. Just to make that statment does not give much information but when one takes into consideration the effect of estrogens and testosterone on the physiology of these growths it almost brings home to us the point that glands and enzymes may be of some practical value in determining the cause of cancer.

I did not hear Dr. Aub say anything about virus. There seems to be much talk, propaganda, and information at the present time available to suggest that a virus is the instigating factor of cancer.

In the nasopharynx and the upper respiratory tract about 18 to 20 per cent of all malignancies occur and I am amazed and disappointed that some of the funds that are available have not been allocated to institutions that deal with these problems. Personlly, in our hospital I know there has been a decided increase in the number of malignancies of the sinuses. We have peculiar types of tumors in the naso-pharynx. I refer to the so-called lymphoepitheliomas. They are either highly anaplastic epitheliomas or reticulum-cell sarcomas. The term lymphoepithelioma is histogenetically confusing and should be forgotten. These tumors metatastasize very early, are quite malignant, respond for a while to radiation, but have a great tendency to result fatally. To state that one can make a

100 per cent accurate diagnosis by the Papanicolaou stain is to me a gross overstatement. I certainly think that the Papanicolaou stain has been an advance in the study of tumors. To place the responsibility on the pathologist to make a diagnosis or not by cytological examination is not just and will lead to many errors.

There has been a recent technique developed which I think is decidedly better than a cytology study. That is the sponge biopsy. Use is made of a piece of gelfoam on a clamp or applicator and you rub this upon a suspected lesion and drop it in formalin. Sections are made just like a tissue biopsy. Gelfoam is a protein substance and lends itself to infiltration and sectioning. One can exert considerable pressure on a mass to denude the surface and then clusters of cells adhere to the sponge.

There is no need today with the mechanical means available to wait a week for the diagnosis on a biopsy. This is particularly true with the small tissues that are taken from the nasopharynx, larynx, or bronchus.

LOUIS H. CLERF, M.D.: I enjoyed Dr. Aub's paper and was interested in his reference to the Papanicolaou smear technique which undoubtedly has added enormously to our diagnostic armamentarium, Dr. Eggston to the contrary.

We used it extensively in bronchogenic carcinoma; the fact that carcinoma is an exfoliating lesion has permitted work in other fields. Dr. Herbut, who works with me, has also been doing a great deal of work in carcinoma of the prostate.

In addition to diagnosing carcinoma of the nasopharynx as suggested by Dr. Aub and practiced by Dr. Morrison, I believe it is an excellent aid in the diagnosis of carcinoma of the nasal accessory sinuses, which also is at times difficult to diagnose without doing areasonable amount of surgical exploration. If one can secure secretions from the nose, and, being familiar with the normal nasal epithelium, there is no reason why an early diagnosis should not be made.

JOSEPH C. AUB, M.D. (closing): Several very interesting points were brought out in the discussion.

First of all about biopsy, whether biopsy is safe or not, I have always been scared of biopsy. The surgeons say that you don't spread the tumors around by means of biopsy but it is obvious that biopsies are so essential that one has to continue to use them and I think one does run a risk in a sloppy biopsy of desquamating cells which may later cause trouble. But one cannot go on with practical handling of neoplastic disease without biopsies unless one can get it by methods such as was suggested by making a diagnosis from desquamated cells.

There was much discussion about the Papanicolaou stain. I brought it up first of all because I think its value in accessory type of secretions is increasing, providing one can get a very prompt specimen on the slide and not use old ones, but the reason I brought it up is much more from the point of view that it gave an indication of how tumors are spreading themselves because of the possibility of desquamation fiom them and therefore seeding themselves around the body and from that point of view it becomes of very great importance in the handling surgically of tumors in so far as one does not want to spread them around.

The virus question came up. There are many ways of producing tumors and I did not mention them. Virus is one of them. There is no question but

what a virus is the cause of chicken tumors. It is getting less and less of a question that virus in milk or virus-like substance in the milk causes neoplasia in mice. There has never been shown to be a virus causing a tumor in man but to my way of thinking a virus is merely one of the ways of the very many ways which we now have of producing the same shift of the cell which shifts it towards unrestrained cell division. The virus has no different effect from the carcinogenic substances, the crystalline carcinogenic substances. They all produce the same result. Therefore the virus just seems to me to be one of the ways of making cells, if you want to say, irritating cells toward malignancy and virus plus crystalline substances like methyl cholanthrene summate so the two are more effective than one. In other words, they both seem to be working on the same mechanism, but that they are the cause of the tumor I would not like to say. I would like to rather say that they stimulate a mechanism which is the mechanism involved in tumors. I think people who are working with virus also agree—and this was brought out in the discussion—that there is much more than the local effect and that there is the effect on the host in general. One sees too much evidence of that in the clinic to ignore it. You cure a prson of one tumor and then he gets three or four others, and one sees patients who have had five distinct types of tumor over a period of years. As one cures one after another, it is suggestive in this work of Huggins also that there is a constitutional factor in the production of neoplasms of which one keeps on cropping up. One of them is apparently the setup in relationship to the internal secretions.

The problem of nucleoprotein was also brought up and that also was important because it is obvious that tumor cells must get their energy from somewhere. You have all seen these moving pictures of dividing cells in tissue cultures. It requires an enormous amount of energy for a cell to divide and tumor cells must get that energy somewhere. From some of our recent work in our laboratory, it is obvious that tumor cells can synthesize protein much more rapidly than normal cells can, but also which fits in with the theory that I stressed, that normal tissues can increase their synthesis of protein. For instance, if one takes the normal liver and determines the amount of nucleoprotein which it can synthesize with a radioactive amino acid, if you feed amino acid and determine the amount of the amino acid which gets incorporated in the protein, you can then take out two-thirds of the liver and you find the liver cells in dividing can then pick up three times the amount of radioactive amino acid which the normally resting liver cells can do, and that work has been done by Dr. Semsig and Dr. Franz in our laboratory, but a hepatoma does not synthesize substance on the average of three times but synthesizes on the average of seven and eleven times as rapidly. In other words, it can synthesize much more rapidly than the resting cell and much more rapidly than normal dividing cells can do, but both can increase speed of synthesis of their own protein. However, the tumor cells have gotten an ability to do it more rapidly than the normal. In other words, the normal cell is on the way to neoplastic cells in that regard although it is not as effective in storing itself the necessary energy for cell division.

PLASTIC REPAIR OF SADDLE-NOSE

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AND

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LOS ANGELES, CALIF.

The history of the plastic repair of saddle-nose reveals that implants have waves of popularity and decline.

Paraffin, which was employed for the first time in 1901 by Eckstein, has been used extensively. Every now and then we see patients who have tolerated it for years with good cosmetic results. Vaselin was recommended by Gersuny[1] as early as 1887. Celluloid, ivory, gold, platinum and aluminum as well as bone and cartilage from animals have been tried and discarded. Ticonium and tantalum have been developed and used recently along with acrylic implants.

These materials are really foreign bodies and they were used in order to obviate the need for another operation.

Cortical bone from the tibia or crest of the ilium was tried and discarded because it absorbed rapidly.

Koenig[2] introduced autogenous cartilage in 1920. It has many advantages but at times it will curl and fail to form a firm union.

Carter[3] thought that a combination of bone and cartilage was necessary in saddle-nose so he used rib implant of bone and cartilage.

Ever since Pierce and O'Connor[4] introduced it in 1938, cadaver cartilage has enjoyed great popularity because it is so readily available. Recently there has been criticism of its use because it is said to absorb readily. Some surgeons have discarded it completely. We

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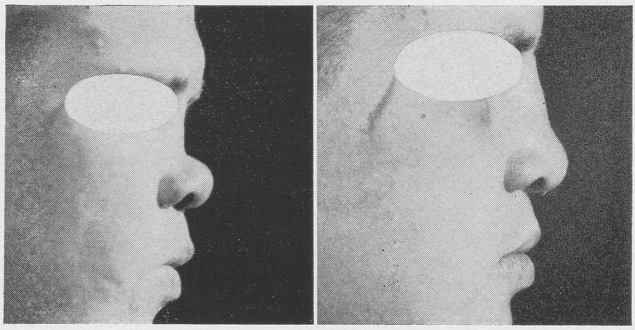
From the Otolaryngological Service of Navy Hospital, Long Beach, Calif.



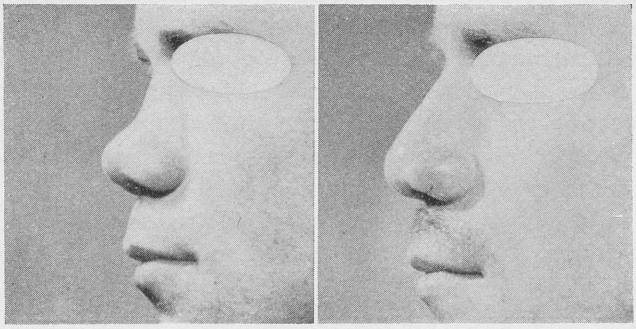
have seen it absorb rather promptly in a few cases and for that reason we decided to try cancellous bone grafts in a series of cases.

Cancellous bone has been advocated because it is highly resistant to infection and absorption and it forms a firm union with the surrounding area.

Recently, Abbott el al.[5] published the results of experiments with cancellous bone used in filling bony cavities. They found that it can be used safely and satisfactorily. They also proved that cancellous bone implants have the ability to regenerate bone. The bone marrow cells undergo rapid degeneration and provide wide channels for the invasion of new vessels and eventually for the accommodation of newly formed bone. It offers an opportunity for regeneration from all surfaces.

Mowlem[6] used cancellous bone from the ilium because of its porosity and high cellular content. He claims that the blood supply appears very early. Macomber[7] believes that all foreign substances should be abandoned. He is convinced that iliac cancellous bone is dependable, most useful and safest of all materials for correction of defects about the face. Gordon[8] employed bone chips in the presence of infection and found that they lived. He placed the chips in contact with bone denuded of its periosteum.

We wish to record our experience with a series of 20 cases of saddle-nose defects in which cancellous bone was used. The bone



was obtained from the ilium in all cases. Casts of the face were made in some cases and photographs in all. The length of the defect was measured with wood which was boiled with the instruments. Local anesthesia consisting of novocain and adrenalin was injected and an incision about three inches long was made under the edge of the iliac crest. The skin and subcutaneous tissues were divided and retracted. The periosteum over the external surface and near the edge of the bone was incised and a sharp chisel unroofed the cancellous bone by chiseling off the cortex and leaving it attached to the periosteum on the inner surface. The cortex was elevated and a gouge inserted to remove the cancellous bone graft which was grasped with a towel clip and stored in saline. The cavity was packed with Gelfoam and the wound closed with chromic catgut and skin clips.

Following the operation there were no infections and no hematomas. The disability following was not marked. The patients complained of slight discomfort. One patient complained of numbness in the right leg and lameness for about six weeks.

On three occasions we had two patients scheduled for implants; each time one donor was used for both implants thus correcting six defects with three donors. No difference in reaction nor in results was noted in these patients.

The bed for the implant was prepared after all necessary surgery on the nose was completed. In most cases it was necessary to frac-

ture the lateral walls inward to narrow the nose and in about one-half of the cases the nasal tip was reconstructed. In most instances the implant was introduced through the vestibule; in a few it was introduced over the alar cartilages. A raw surface was obtained by rasping or elevating the periosteum. The implant was molded with the aid of an electric bur. While the operator held the bone with a towel clip and a wet sponge the assistant operated the bur. The implant was held in place by adhesive straps and a tantalum splint. In a few cases a mattress suture of fine Dermalon was used to hold the splint in position.

CONCLUSIONS

Our experience shows that the bone implant "takes" readily and seems to form a firm union quickly. A few days following surgery the implant is firmly fixed with a very little reaction in the tissues. It appears to form an integral part of the nose within a week. No signs of absorption were noted in cases seen two years after the operation. The patients with bone implants from another donor had equally good results. We recommend the electric bur for modeling the implant.

6777 Hollywood Blvd., Hollywood.

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DISCUSSION

SAMUEL SALINGER, M.D.: The old adage that you can skin a cat in many different ways applies to this particular situation. Over a period of thirty years I have experimented with all types of implants and I have come to the conclusion that in the order of preference I would take first, autogenous costal cartilage; second, autogenous bone; third, preserved cartilage, and fourth, foreign substance.

Some years ago I reported a series of 125 cases where I had implanted ivory, 15 per cent of which were lost through infection or by extrusion. With the advent of preserved cartilage I gave up using ivory. I can tell you that today there are instances in which I use ivory with great success where other materials have failed. You know that there is no guarantee even if you use autogenous costal cartilage that it will be retained or will not curl. I was chagrined at one time to see an illustration in an article by a plastic surgeon of a young lady whom I had operated on years before, using an autogenous costal graft with a very successful result. Yet the picture showed this graft twisted out of shape, producing a marked deformity. The author, one of our best men, removed the autogenous graft and replaced it with preserved cartilage. Since then I have had the same experience in which an autogenous graft had failed and in which, subsequently, a preserved cartilage graft was successful.

My objection to the bone graft is that it forms too rigid a nose. The fact that it grows into the bed produces too much rigidity so that the nose is not susceptible to normal movements and accidental displacements inherent in its exposed location.

I have a slide here showing a young man in whom three successive operations were failures, the first an autogenous and then two preserved cartilage grafts. One failed through infection and two through foreign body reactions. As the result of these reactions he had quite a marked retraction and depression of the tip. I do not know of any material that will force a tip up into its normal position once scars have formed in it. Cartilage isografts will hold very well in the dorsum but most of the struts which I have placed in the columella for the purpose of raising a tip which has been pulled down by a scar have failed. In this instance I went back to ivory and was successful. This was done two years ago and the result is still good.

(Slide) This x-ray picture shows the two pieces of ivory which are interdigitated in such a manner that they are locked but still capable of being moved with the tip of the nose. I still see some of my ivory cases of 20 and 25 years ago, which are apparently being tolerated without reaction.

FRED Z. HAVENS, M.D.. In general, I prefer cartilage rather than bone for repair of the saddle nose because a bone graft makes the nose too rigid. Even in

those cases in which repair with cartilage requires the use of a columellar strut the nose, while quite rigid, is not as much so as when the repair is made with bone. In those cases in which a columellar strut is not needed a highly satisfactory correction often can be made with cartilage and the normal flexibility of the nose retained. There will, of course, be occasions in which bone will be preferable because of some special problem and in such cases it should be used.

I prefer to use cartilage from the patient's own rib. The problem of curling can be overcome in most instances by simmering the cartilage as has been described by Doctor New. Note that we say "simmer," not boil. The solution with the cartilage in it is kept just hot enough so that the small bubbles can be seen rising to the surface. This temperature is maintained for 20 minutes and in order to do this correctly it is necessary to have someone give the simmering beaker his constant attention for that entire time. I have observed cartilage that curled after such simmering but only rarely.

EDWARD D. KING, M.D. (closing): I agee with Dr. Salinger and Dr. Havens that the nose feels a bit hard and unnatural following bone implants. However it looks extremely well and that is what the patients are interested in.

One of my colleagues has suggested that if cadaver cartilage was inserted in the abdominal wall for a period of two or three months it can be used safely. I tried this on one patient in whom the cartilage had absorbed rapidly and it has remained in place for over a year without any absorption. It is a great temptation to use cadaver cartilage in all cases because it saves the patient time and a second operation. It is too bad that it is not as satisfactory as other implants.

HEMILARYNGECTOMY: METHOD OF MAINTAINING A SATISFACTORY AIRWAY AND VOICE

HENRY M. GOODYEAR, M.D.

CINCINNATI, OHIO

Tumors of the larynx which are too extensive to be removed by cordectomy or laryngofissure but would be satisfactory for hemilaryngectomy, are not so treated since contraction of the glottis in healing is so great that the airway is useless; a permanent retention of the tracheotomy tube is necessary; thus, a total laryngectomy is the only practical procedure to follow, even though a part of the larynx might have been saved without any great danger of recurrence.

However, with the assurance of an open glottis, with ample breathing space and a useful voice minus an annoying tracheotomy opening, many patients can look with greater complacency upon an extensive operation of the larynx.

Even after total laryngectomy and healing, biopsy will reveal that the contracted scar tissue closing off the normal airway is only 1-2 cm. in length and is the chief obstacle to an airway between the trachea and the hypopharynx. I have been surprised at how near and yet how far this short barrier places the open trachea.

Some 16 years ago in an attempt to overcome this barrier following a total laryngectomy I sewed a large piece of rather heavy rubber tubing in this area as an obturator at the time of operation. The upper end of the tube was closed with sutures and the open end was in contact with the tracheotomy tube. This tube was removed six weeks after operation, and a urethral sound was used for some weeks later through the tracheal wound to maintain an open tract to the hypopharynx. This man, now aged 79, is still living and well (16 years after operation). By placing a finger over the tracheal opening he is able to converse and on several occasions has talked to me over the telephone. The opening, however, is not of sufficient size for breathing.

After a number of years I was convinced that an ample airway could be obtained if a continuous tract of mucous membrane, even though narrow, could be maintained at operation between the trachea and the hypopharynx without undue risk of recurrence of the tumor.

I believe you will agree that given a carcinoma of one cord, with its removal by laryngofissure, recurrence does not occur in the opposite cord except by extension through the anterior commissure. Few surgeons have even seen a carcinoma in the interarytenoid space. There may be recurrence in the anterior pretracheal muscles as well as in the glands along the carotid sheath or the lateral pharynx or the mouth of the esophagus, but the opposite cord which was clean at the primary operation may still be smooth save for extension across the anterior commissure.

Where I have found carcinoma involving both cords I have also been able to find malignant tissue in the anterior commissure.

I shall cite the maximum of tumor extension in which I would attempt or advise a hemilaryngectomy.

If one-half of the larynx is free of any visible evidence of carcinoma even though the arytenoid on the opposite side is fixed, a hemilaryngectomy may be safely performed. A fixed cord may contra-indicate laryngofissure but not hemilaryngectomy.

Operation. Under local anesthesia or a cervical block the larynx is opened in the midline. Careful examination is made as to visible extension of the tumor. An incision is made in the midline in the interarytenoid area or slightly to the normal side. This incision is carried downward over the cricoid, or at least 1 cm. or more below the visible edge of the tumor.

Where the anterior commissure is involved it is my practice to remove normal cord tissue well beyond the lesion with cartilage, epiglottis, and all pretracheal muscle tissue in this area. I agree with Schall[1] that these muscles are rich lymphatic beds. This area is also rather severely cauterized which may produce some sloughing later. I have often felt this sloughing may be a blessing in disguise in further removal of questionable tissue.

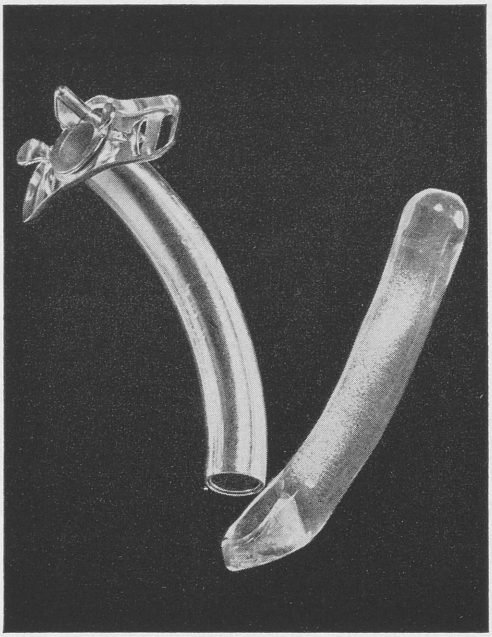

Fig. 1.—Acrylium obturator.

The wing of the thyroid cartilage on the affected side is widely resected (not subperichondrially) including the arytenoid. Examination for lymph glands along the carotid is made at this time and a wide resection done if necessary.

After all bleeding points have been cauterized or ligated an attempt is made to line a part of the denuded area by drawing in and suturing mucous membrane from the region of the hypopharynx and the mouth of the esophagus. Similar use of mucous membrane to cover denuded areas in laryngofissures shortens convalescence.

A solid acrylium tube (Fig. 1) 9 cm. (3½ in.) long and 13 mm. in diameter (the diameter of a No. 8 tracheotomy tube), with one end perforated to fit over the convex curve of the tracheotomy tube, is placed in the larynx. The tube must rest firmly against the tracheotomy tube to prevent a fibrous membrane intervening, as may occur where wire or a metal stirrup is used.

The mucous membrane is now sutured about the upper portion of the tube, but not over the end of the tube which extends freely upward into the pharynx and can later be readily seen with a pharyngeal mirror standing like a post at the base of the tongue, yet there is no complaint of irritation or coughing, or dysphagia, even though it may be worn for months.

The deep tissues and skin are closed without drainage.

A feeding tube is passed through the nose prior to the placing of the acrylic tube.

The acrylic tube must be worn for a sufficient length of time to permit the glottis to become lined with mucous membrane and to permit the surrounding tissues to heal and contract against the tube and form a dense hard wall of scar tissue. During the healing process the patient will speak by air escaping around the obturator when a finger is placed over the tracheotomy opening.

In the light of recent investigation carried on by Brown and McDowell[2] concerning the growth of mucous membrane in the trachea, I am led to believe that the good results previously obtained in operations for laryngeal stenosis were due to leaving the obturator for a sufficiently long time to permit the skin grafts to be replaced by mucous membrane.

The skin grafts as shown by Brown and McDowell do not undergo metaplasia, that is, transformation into mucous membrane. The skin is eventually replaced by ingrowing mucous membrane.

After hemilaryngectomy I have seen an excellent glottis when the obturator was worn but two weeks, but prefer to wait ten to twelve weeks before removing the tracheotomy tube and the acrylium obturator which is removed through the tracheotomy wound.

Selection of Obturator. Inert, nonirritating material plus the proper length and diameter constituted the chief problems in obturators. First, rubber tubing, then vulcanized rubber material were tried. Acrylium seems to be very satisfactory but it will not withstand boiling and alcohol also affects it.

At first, silver wire was used and sutures were passed through perforations in the tube and carried through the soft tissues of the neck in order to hold the obturator in place. This procedure proved unsatisfactory. The tube was then fastened to the tracheotomy tube by means of silver wire. This method was also unsatisfactory. A small metal stirrup will suffice but an acrylium obturator, with a perforation for the tracheotomy tube in the slightly curved end reduces granulations in this area, which is important.

Should a separation of skin over the tube occur during healing it must be reclosed by sutures.

The establishment of a successful airway to the hypopharynx following total laryngectomy has not yet been accomplished, but it can now be done where more than one-half of the larynx has been removed.

Even in laryngofissures where the arytenoid has been widely removed, an obturator worn for two to six weeks will insure a much freer breathing space and fewer granulations.

The recent work of Daniel[3] has been most interesting and instructive on the regeneration of the trachea and bronchi in dogs. Metal or glass tubes were used to bridge the defect and a new tracheal or bronchial wall developed, lined with epithelium; even well-developed cartilaginous rings were formed, not from pre-existing cartilage, in a certain number of animals.

SUMMARY

I have shown that it is possible to establish an open tract between the trachea and hypopharynx after total laryngectomy, permitting the patient to speak.

I have presented an obturator which, when used at hemilaryngectomy, will assure an ample airway for breathing and for speaking after complete healing.

556 Doctors' Building.

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DISCUSSION

LOUIS H. CLERF, M.D.: I am greatly interested in Goodyear's presentation. When he closes I would like to have him give us his statistical data. I realize of course this is a recent procedure and he probably has not a great group of cases nor have they had an opportunity to live a long time. In one case a block dissection was done. I question whether I would have the courage to leave the other side of the larynx behind in such a case. I must admit with what I have seen of carcinoma one cannot be too radical in its surgical treatment, and, while conserving an airway and all that is important, as Dr. Aub said, the first plan of therapy is the most important. Unless one can attain one's objective then one never quite catches up with the carcinoma.

GORDON B. NEW, M.D.: Dr. Goodyear certainly apparently has a new idea. As Dr. Clerf has brought out, I would like to know the microscopic grade of the tumor he is dealing with in this operation because as our Guest Speaker this afternoon brought out, we cannot manipulate tumors and not expect to get metastases. If it is a highgrade tumor, I am afraid there is a good chance of metastasis. I prefer to use surgical diathermy in the removal of these growths as I feel that the patient has a better chance of getting well than he would have with a knife or scissor excision. The secondary scarring that Dr. Goodyear referred to can be removed and replaced with a skin graft on a soft rubber mold as I have brought out on previous occasions. I have had three patients return recently who have had skin grafts of their larynx and trachea for over three years and the skin is still present.

Dr. Goodyear should be congratulated on this new idea. If the end results are as good as the immediate ones, it should be an excellent plan.

HENRY M .GOODYEAR, M.D. (closing): I wish to thank Dr. Clerf and Dr. New for their discussions.

I realize that this is a new and radical procedure and only time and statistics can tell how satisfactory it will be. From my observation, a patient who has a normal half of larynx, even with metastases to the neck, and who dies later from cancer, will show at autopsy or on examination before he dies that the side of the larynx which was free from growth at the time of operation may also be free from growth at the time the patient dies.

My argument here is for saving some normal tissue, which often exists on the opposite cord, and this operation is recommended for cases in whom one cannot do a laryngofissure safely but where a slightly more radical procedure

may suffice and at the same time be done without any greater danger of metastasis than with laryngectomy. I agree with Dr. New that electrocoagulation is of help in these cases and I use it on the edges of the excision and in the tissues anterior to the lesion, where there is extension into the anterior commissure.

As to the skin graft, I may be wrong. In some of the cases that we have observed in which an operation has been done for laryngeal stenosis, the skin after a year or two has been largely replaced by mucous membrane. I think it would be very interesting to know whether this occurs uniformly or whether these people retain the skin that was implanted over a great number of years.

PRESENTATION OF INSTRUMENTS

AN IMPROVED LARYNGOSCOPE

Edwin N. Broyles, M.D.

Baltimore, Md.

When doing a direct laryngoscopy under local anesthesia, sometimes there is difficulty in exposing the anterior portion of the larynx due not so much to the space down around the larynx itself, but to large teeth and a short neck. For this reason it seemed that perhaps it would make these examinations easier on the operator and much more comfortable for the patient if we could have a laryngoscope with a small proximal end and a large distal end and one that gives good vision and also a wide operative field. With this in mind we had a laryngoscope made with a small proximal end and a large distal end; also to increase our vision and to give a better means for close examination we have devised a small proximal magnifying system which tips over the proximal end of the laryngoscope. These are manufactured by the A.C.M.I. Company. The proximal magnifier will also fit on the bronchoscope and esophagoscope.

IMPROVED LARYNGOSCOPE FOR INFANTS EQUIPPED WITH AN OXYGEN INSUFFLATION APPARATUS

Gabriel Tucker, M.D.

Philadelphia, Pa.

APPARATUS TO RECORD THE APPEARANCE OF THE SUBGLOTTIC LARYNX BY PHOTOGRAPHY

Gabriel Tucker, M.D.

Philadelphia, Pa.

Memorials

LIONEL COLLEDGE

1883-1948

Mr. Lionel Colledge, a Corresponding Fellow of the American Laryngological Association since 1940, died in London, England, December 19, 1948.

He was born in Cheltenham, Gloucestershire, England, on October 5, 1883. His father was Major John Colledge, Bengal Lancers, Indian Cavalry, and his grandfather, Thomas Richardson Colledge had been Surgeon to the East India Company; his mother was Jane Mackenzie Inglis of Kingsmills, Inverness, Scotland. His early life was spent in Cheltenham and he was educated at Cheltenham College from which he graduated in 1896. He then entered Caius College, Cambridge, completing his course there in 1900. Graduating in medicine at London University in 1908 with L.R.C.P., he later received the degree of M.A.M.B. from Cambridge and qualified for M.R.C.S. As an intern at St. George's Hospital he served for two years in Medicine, Surgery and Gynecology, and graduated with the degree of M.B. In 1910 he received the degree of B. Ch., and took the F.R.C.S. a year later.

During the 1914-1918 war, he served with the R.A.M.C. in France, and after a short period in command of a casualty clearing station he became Aural Surgeon to the First Army. In the recent war, Mr. Colledge came to the assistance of St. Mary's Hospital and at the same time acted as consulting otologist to the Royal Navy.

He was on the staff of the Hospital for Diseases of the Throat in Golden Square, and he was Consulting Surgeon to the Ear and Throat Department in St. George's Hospital. Later he was also Surgeon to the Royal Masonic Hospital and the West End Hospital for Nervous Diseases. The rules of St. George's Hospital made it necessary for him to retire at the height of his professional activity, but his election to the staff of the Prince of Wales General Hospital at Tottenham allowed him to continue his hospital work there. In later years he acted as consultant to the Cancer Hospital, where he was able to continue his work on malignant disease of the larynx and pharynx—a work which he had begun early in his career in association with Sir St. Clair Thomson. Together they published in 1930

a monograph on cancer of the larynx which was one of a series in the Anglo-French Library of Medicine and Biological Science. This work included the material which had already been presented by Colledge as Semon Lecturer in Laryngology at the University of London in 1927. His long association with University College Hospital was terminated only by his death.

He contributed articles to the British Encyclopedia of Medical Practice and to Maingot's Postgraduate Surgery, and wrote authoritatively on a variety of subjects with a wide knowledge of the literature of his specialty. His Guide to Diseases of the Nose and Throat was written in collaboration with C. A. Parker, and his work on the surgical treatment of paralysis of the vocal cords, in which he assisted Sir Charles Ballance, is well known. The pioneer work on nerve anastomoses appeared in the British Medical Journal during 1927 and 1928.

Mr. Colledge was one of the founders of the British Association of Otolaryngologists and its first vice-president, and he held the presidency of the Section of Otology and Laryngology of the British Medical Association at Oxford in 1936, of the Section of Laryngology of the Royal Society of Medicine in 1936 and 1937, and of the Section of Otology of the Royal Society of Medicine in 1940. He was a member of the Societe de Laryngologie des Hopitaux de Paris and of the Association Cientifica del Institute Hispano- Amercano de Otorhinolaryngologie.

In 1917 he married Margaret, the daughter of the late Admiral J. W. Brackenbury, and they had two children. Their son Maule lost his life in the late war serving with the Royal Air Force in Europe. Their daughter Cecilia is world famous as a skater.

He was a member of the Union Club and the Trafalgar Square Club. His diversions were mainly shooting and fishing.

Lionel Colledge was known internationally and was one of the most distinguished figures in otology and laryngology in England. For many years he was a valued contributor to the British Medical Journal.

SECORD HERBERT LARGE, M.D.

1872-1949

Secord Herbert Large, an Emeritus Fellow of the American Laryngological Association, died at Cleveland, Ohio, on March 9, 1949. He was 78, and had retired from active practice in 1942.

Born on February 17, 1872, in Kincardine, Ontario, Canada, he was the son of Rev. Richard W. Large, a Methodist minister, and Martha Cunningham Large. His preliminary education was obtained at public schools and the Weston Institute, and he was a graduate of Trinity College and of the Medical School of the University of Toronto (1893). After serving an internship at the Childrens' Hospital, he spent several years of practice in Canada, and later began the study of laryngology at the National Eye, Ear, Nose and Throat Hospital, Dublin, Ireland. After spending two years at clinics in Vienna, Berlin and Paris, he began the practice of his specialty in Cleveland in 1904.

Doctor Large was a founding member of several national societies and for 31 years was treasurer and comptroller of the American Academy of Ophthalmology and Otolaryngology. He was honored by that society with a plaque for his accomplishments in his field and for his services to the organization. He was also a Fellow of the American Medical Association and the American College of Surgeons, and a member of the American Laryngological, Rhinological and Otological Society, Cleveland Academy of Medicine, the Cleveland Otolaryngological Club, the Pasteur Club, the Union Medical Club and the American Broncho-Esophagological Association.

Doctor Large's hospital activities were largely confined to the Lakeside and St. Vincent's Hospitals in Cleveland. He was a prolific contributor to otorhinolaryngologic literature and became keenly interested in broncho-esophagology. Much of his reesarch in early years was concerned with the causation of the common cold and he later was active in perfecting the technique of tonsillectomy.

In 1907, he married Helen Rainey of Cleveland, Ohio, who survives him. This union was blessed with two girls and two boys.

Doctor Large was a member of the Cleveland Country Club, the Union Club and the Kirtland Club. In politics he was a Republican and he was a member of the Presbyterian Church. His principal diversions were books and out-door sports.

As a pioneer in the field of otolaryngology in Cleveland, Doctor Large was ever progressive and maintaining his interest in his specialty by frequent trips to European clinics and by his active participation in the affairs of national societies.

SAMUEL McCULLAGH, M.D.

1876-1948

Samuel McCullagh was born in Philadelphia on February 21, 1876, and died on July 21, 1949. His father was a clergyman, Archibald McCullagh, who had been born in Armagh, Ireland. His mother was Ella S. Kerr of Philadelphia.

Doctor McCullagh was elected to Fellowship in the American Laryngological Association in 1921 and became an Emeritus Fellow in 1943. His early life was spent in Philadelphia, Brooklyn and Worcester, Massachusetts. From 1886 to 1891 he received his preliminary education at the Worcester Academy and the Brooklyn Polytechnic Institute. Entering the University of Pennsylvania in 1891, he received the degree of Bachelor of Arts in 1895 and the degree of Doctor of Medicine in 1898.

After serving an internship at the Childrens' Hospital of Philadelphia, he served as an intern at the Hospital of the Protestant Episcopal Church from 1898 to 1900. During the next year he was in charge of the Girard College Infirmary. He then became associated with the Manhattan Eye, Ear and Throat Hospital and the Polyclinic Hospital in New York City where his professional life was spent.

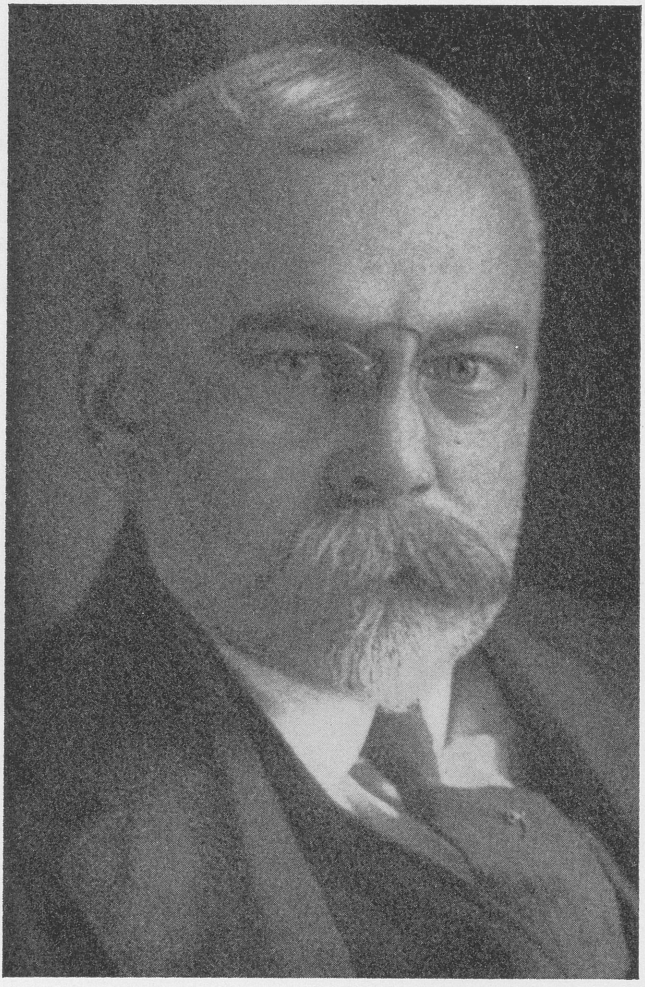
He was a former president of the New York Medico-Surgical Society and of the New York Laryngological Society, and had served as Chairman of the Section on Laryngology of the New York Academy of Medicine. In addition to Fellowship in the American College of Surgeons, he was a member of the American Laryngological, Rhinological and Otological Society, the New York Academy of Medicine, the New York Otological Society, the New York Laryngological Association, the American Laryngological Association and the American Medical Association.

Doctor McCullagh was a member of the University Club, Nassau Country Club, University of Pennsylvania Club and Phi Gamma Delta. He was a staunch Presbyterian and a Republican in his political views. His principal diversion was golf.

In 1916, he served on the Mexican Border as a medical officer of Squadron A. During World War I he served in France as a Lieutenant Colonel in the Army Medical Corps and received the Distinguished Service Medal because of outstanding service.

On May 24, 1906, he married Grace M. Thompson of Hudson, N. Y. There were no children.

From 1903 to the time of his retirement, Doctor McCullagh was one of the outstanding otolaryngologists of New York City. As Consulting Laryngologist to the Manhattan Eye, Ear and Throat Hospital, he continued an unusually successful teaching career.



JAMES F. McKERNON, M.D.

1865-1949

James F. McKernon, a Corresponding Fellow of the American Laryngological Association, died on January 22, 1949. He was born on March 13, 1865, in West Cambridge, New York, a son of John Cochran and Jane (Dalland) McKernon. The McKernon family is of Scottish origin, while the family of Doctor McKernon's mother was originally native to the North of Ireland. His father was born in Elgin, Scotland, where the family had been established for many generations, and whence John Cochran McKernon and his three brothers emigrated to America, where all four served in the Federal Army during the Civil War.

The early education of Doctor McKernon was obtained in the district school of West Cambridge, New York, and the Greenwich Academy, Greenwich, New York. This was supplemented by a further study period of two years under private tutors. He received the Degree of Doctor of Medicine from the College of Physicians and Surgeons in 1890.

Doctor McKernon held many important appointments in public and private institutions in New York City, among which may be cited: 1890 to 1892, Physician in Charge, Berachah Mission Dispensary; 1892 to 1897, Assistant Surgeon, Throat Department Manhattan Eye and Ear Hospital; 1893 to 1896, Assistant Surgeon, Aural Department, New York Eye and Ear Infirmary; 1897 to 1900, Assistant to the Chair of Otology, Bellevue Hospital Medical College; and in addition acted as Aural Surgeon to the New York Eye and Ear Infirmary, and Professor of Otology, New York Post-Graduate Medical School and Hospital. He was an Honorary President of the Medical Society of New York and of the Board of the New York Post-Graduate Medical School and Hospital. From 1912 to 1914 and from 1920 to 1928 he served as President of the Board of the latter institution, and as the Chairman of a committee of four, brought about an agreement signed on January 14, 1931, between the Trustees of Columbia University and the New York Post-Graduate Medical School and Hospital, establishing a teaching relationship with Columbia University, effective July 1, 1931.

Doctor McKernon was a Past President of the American Laryngological, Rhinological and Otological Society, the American Otological Society and the New York Medical Society. In 1919, he was elected a Corresponding Fellow of the American Laryngological Association.

In 1908, he joined the Medical Reserve Corps of the U. S. Army with the rank of Lieutenant, and in June 1917, he was appointed a Captain and entrusted with the formation of Base Hospital No. 8, consisting of 156 corpsmen, 75 nurses and 30 medical officers. The unit embarked for France on July 15, 1917, aboard the SS. Saratoga which was wrecked and sank at sea the following day. Reembarking on the SS. Finland on July 31, 1917, the unit was attacked by submarines off Belle Isle but reached St. Nazaire, France on August 21, 1917. After establishing Base Hospital No. 8 at Savenay, he was transferred to the Third Army of the British Expeditionary Force and later became Consultant to the A.E.F. for Ear, Nose and Throat Surgery. For his devotion to duty and willingness to work in any capacity, he was promoted to Colonel in the Medical Corps and was awarded the Distinguished Service Medal. From January 22, 1919 to February 11, 1919, he was on duty in the Surgeon General's office in Washington.

In the course of his busy career, Doctor McKernon enriched the literature of his specialty with numerous articles concerning otitic infections and their intracranial complications. The complete mastoid set which he invented came into general use and was adopted by the Medical Corps of the U. S. Navy and U. S. Army.

He was interested in sports and maintained a membership in the New York Athletic Club and the New York Yacht Club.

On June 26, 1901, Doctor McKernon was married to Anna Madeleine Wittmeyer, daughter of the Reverend A. V. Wittmeyer, Rector of the French Huguenot Church, New York City. He is survived by his wife and three children, John Woolsey, Elizabeth and James Francis, Jr.

JOHN BEEKMAN POTTS, M.D.

1876-1948

Dr. John Beekman Potts was born in Morrisonville, Illinois, on July 14, 1876 and died in Omaha, Nebraska, on October 29, 1948.

His early life was spent in Morrisonville, Illinois, were he obtained his preliminary education, graduating from the Morrisonville High School in 1902. From 1902 to 1907, Dr. Potts attended the University of Nebraska and in 1907 was granted the degree of Doctor of Medicine from the University of Nebraska College of Medicine. Following graduation, he was associated with Doctor Harold Gifford and began his long association with the Dispensary of the University of Nebraska College of Medicine. Becoming Associate Professor of Otolaryngology at the University of Nebraska soon after graduation, he later became Professor of Otolaryngology and Bronchology at his alma mater, and since 1937 was Emeritus Professor of Otolaryngology and Bronchology. He was Surgeon in Charge of the Ear, Nose and Throat Department of the Bishop Clarkson Memorial Hospital from 1913 to 1935, and Chief of Staff of the Nebraska Methodist Hospital and Hospital of the University of Nebraska College of Medicine.

Admitted to Fellowship in the American Laryngological Association in 1931, Doctor Potts was also a Fellow of the American Medical Association. He was a member of the American Academy Ophthalmology and Otolaryngology and of the American Laryngological, Rhinological and Otological Society, serving as Chairman of the Midwest Section of the latter in 1928 and 1929.

During World War I, Doctor Potts served as a Captain in the Medical Corps of the Army of the United States from 1917 to 1919 and was in charge of the Center for Otolaryngology and Head Wounds, Allergy, near Chalon sur Soane France.

He was married to Goldie Claire Goddin of Barhamsville, Virginia on June 28, 1913.

Doctor Potts attended the First Congregational Church of Omaha. He was a member of the Omaha Club and the Omaha

Country Club. His hobbies embraced medical history, the collection of old medical books and travel. Golf was his principal diversion.

His first contribution to the literature appeared in the Journal of the American Medical Association in 1913, entitled "Some Comparative Measurements of the Skull and Sella Turcica." This was followed by 24 major articles during the next 27 years. Much of his research activity was concerned with investigations of the role played by chronic hyperplastic sinus infection in bronchial asthma and he was an authority on the intracranial complications of otitic disease. He became an Emeritus Fellow of the American Laryngological Association in 1942.

ERNST CARE SCHMIEGELOW, M.D.

1856-1949

Professor Ernst Care Schmiegelow, elected a Corresponding Fellow of the American Laryngological Association in 1896, died at Copenhagen, Denmark, on February 28, 1949. He was a remarkable figure in the world of otolaryngology. Not only was he the first in Denmark to hold a professorship in this field, but he was also the first to wrest otolaryngology as a specialty from the general surgeons, and these distinctions came to him very early in his career. When a few years ago, at the age of 90, he published his autobiography, based on his diary, he succeeded in painting a vivid picture of the world of medicine in a great part of two centuries. An indefatigable traveler and participator in international medical conferences, this urbane Dane came to know and be known by the leading medical men throughout the world, and his younger fellow countrymen soon learned that letters of introduction from him opened countless doors abroad.

He was born on October 13, 1856, at Rönne, Bornholm, Denmark. His father, Christian, was a sea captain and the son of a physician, while his mother, Marie Dorothea, was an accomplished musician and the daughter of an Army Major. His early life was spent in Copenhagen and from the University of Copenhagen he obtained the degree of Bachelor of Arts in 1873 and the degree of Medicine in 1879. After a two year internship on a rotating service at the University Hospital, he began the study of laryngology in London under Sir Morell Mackenzie.

After leaving London, he spent a number of years on the continent, studying with Fauvel in Paris, with Politzer, Graber, and Storch in Vienna, and with Voltolini in Breslau. When in 1883, Schmiegelow opened a polyclinic for patients with diseases of the ear and throat in Denmark, the surgeons did their best to put him out of countenance. In spite of all opposition he soon became chief of service at the Municipal Hospital, the University Hospital and St. Joseph's Hospital in Copenhagen. From 1889 to 1926, a period of 37 years, he was Professor of Otolaryngology at the University of Copenhagen.

In 1928, Schmiegelow's standing in his own specialty was officially recognized by his selection as President of the First International Congress of Otorhinolaryngology which was held in Copenhagen largely as a result of his efforts. From 1916 to 1917 he was President of the Medical Society of Copenhagen and from 1919 to 1922 he was President of the Danish Medical Society. He held honorary membership in the British Medical Society, the Gesellschaft Deutscher Hals, Nasen und Ohren-artze, the Laryngologischer Gesellschaft in Berlin, the Otolaryngologischer Gesellschaft of Bucharest, the Otorhinolaryngological Societies of Leningrad, Warsaw and Vienna, the Postgraduate Medical Association of America, and the Danish Otolaryngological Society.

Many honors were conferred upon him including elevation to Commander of the Danish Dannenenbrog, Commander of the Swedish Nordsherne, Commander of the Russian St. Stanislaus, Officer of the Legion of Honor (France) and the golden "Bene Merento Medal" from the Pope.

He was a Lutheran and in politics a conservative. In 1884 he married Dagmar Ohsen, daughter of the Danish Consul in Cardiff, England. They had five children.

Professor Schmiegelow was the author of nine textbooks and from 1884 to the time of his death he yearly contributed many papers in English, French, German and Scandinavian. He was co-editor of the Acta Otolaryngologica.

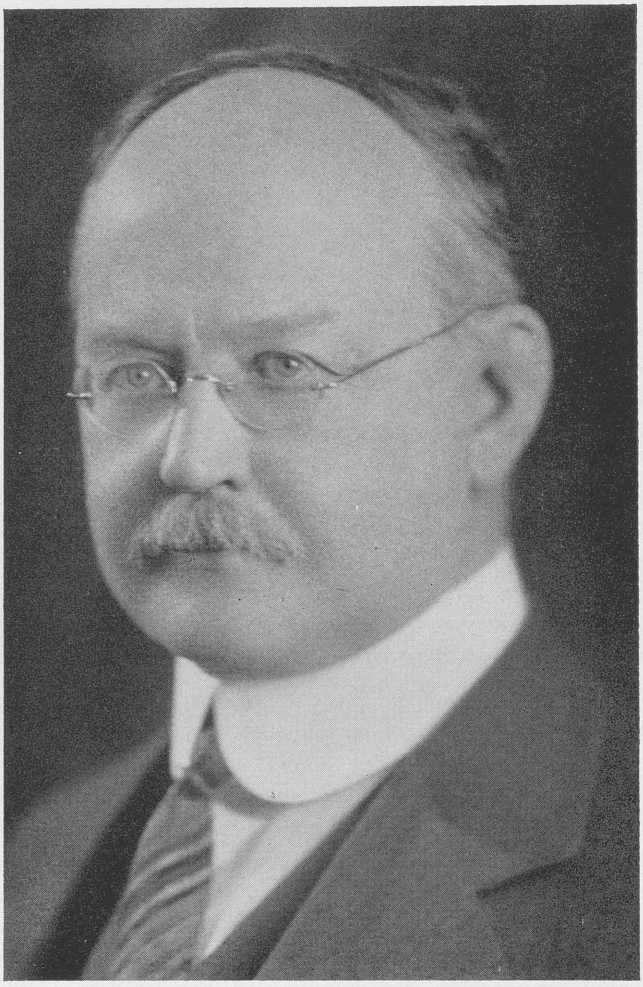
JOHN GORDON WILSON, M.D.

1866-1948

John Gordon Wilson, professor emeritus of otolaryngology at Northwestern University Medical School in Chicago, died at the Putnam Memorial Hospital in Bennington, Vt., August 13, 1949, of cerebral hemorrhage. He was elected to Fellowship in the American Laryngological Association in 1908 and became an Emeritus Fellow in 1939.

Doctor Wilson was born in Edinburgh, Scotland, December 10, 1866. His preliminary education was obtained at the Normal School, Edinburgh. The degree of M.A. was received from the University of Edinburgh in 1887 and in 1890 he received the degrees of M.B. and C.M. from the University of Edinburgh Faculty of Medicine. The next two years were spent in Vienna where he studied the diseases of the ear, nose and throat with Politzer and others, and the pathology of these diseases with Professor Weichelselbaum. Later he spent a few months in Freiburg with Killian. Upon his return, he settled in Glasgow, Scotland, where he was appointed surgeon to the Bellahouston Dispensary and the Victoria Infirmary Dispensary. In 1900 he was at Strasbourg studying the physiology of the ear with Professor Ewald and the vital staining of tissues with Bethe.

In 1901 he accepted the position of instructor in the anatomy department of the University of Chicago, and in 1905 became assistant professor of anatomy. For several years after his appointment to the University of Chicago, he spent each alternate summer in London in the laboratory of Doctor Mott, investigating peripheral nerves and nerve-endings in human tissue. As an outcome of these investigations the following papers were published: The Taste Buds in the Larynx of Man, published in Brain (1905); The Nerves and Nerve-endings in the Membrana Tympani of Man, published in the Journal of Comparative Neurology and Psychology (1907); The Nerves and Nerve-endings in the Heart Muscle and Coronary Blood Vessels of Man, read before the Royal Society of London and published in their Proceedings in 1909. Early papers published in the Transactions of the American Laryngological Association included: Variations of the Ostium Frontale; Comparative Anatomy of the Larynx in Anthropoidea; Plasma Cells in Tonsils; and the Etiology of Pansinusitis.



In 1908 he joined the faculty of Northwestern University Medical School as professor of otology, becoming professor of otolaryngology and chairman of the department in 1924, and retiring in 1945 with the rank of professor emeritus.

During World War I he served as a Lieutenant-Colonel in the Canadian Expeditionary Forces from 1915 to 1917. After returning from the war and his subsequent appointment to the Vestibular Committee of the National Research Council, his papers dealt especially with the ear, its function and its intracranial connections. In 1931 he read a paper before the American Laryngological Association on laryngeal vertigo and its relation to cataplexy.

Doctor Wilson was Chairman of the Committee on Vestibular Reesarch of the National Research Council from 1920 to 1928, Chairman of the Committee on Aural Structure and Function from 1920 to 1930 and Chairman of the Otological Research Bureau from 1936 to 1938. He was a past president of the Institute of Medicine of Chicago and of the American Otological Society, a member of the American Laryngological, Rhinological and Otological Society, a member of the American Anatomical Society, a fellow of the American College of Surgeons, an honorary member of the Harvey Society of New York, a member of the Illinois Medical Society, a member of the American Association for the Advancement of Science and of the National Research Council, and a member of the Collegium Oto-Rhino-Laryngologicum Amicitiae Sacrum.

He married Lilias Aimers in 1901. There were no children. Doctor Wilson was a Presbyterian. His principal diversions were fishing and the study of the history of medicine. He was an inspiring teacher and his energy and enthusiasm were responsible for the initiation of much basic research activity. Each of more than 70 articles contributed to the literature indicate the thoroughness of his investigations and the soundness of his conclusions. He was largely concerned with providing a sound anatomical basis for otological research and his success in this direction is his own best monument.

Doctor Wilson was formerly on the staffs of the Passavant Memorial and Wesley Memorial hospitals in Chicago. He was the author of a history of the medical schools of America in the 18th century, and a medical history of Edinburgh University in the same period as well as of numerous other publications.

V. VISSCHER WOOD, M.D.

1886-1948

V. Visscher Wood, an Active Member of the American Laryngological Association, died on June 20, 1948, at St. Louis.

Born in Pettis County, Missouri, on November 24, 1886, he spent his early life near Sedalia and Warrensburg, Missouri. His preliminary education was obtained in the public schools of Warrensburg and the Warrensburg State Teachers College. After obtaining the degree of doctor of medicine from the Washington University School of Medicine at St. Louis, Mo., in 1913, he served an internship at the Washington University Hospital and became house surgeon at the Frisco Hospital, St. Louis, during the next four and one half years. His long association with Doctor W. E. Sauer began in 1919.

He was instructor in otolaryngology at St. Louis University from 1924 to 1931, senior instructor in otolaryngology from 1931 to 1938 and assistant professor of otolaryngology from 1938 to the time of his death. His hospital positions included: otolaryngologist, Mullanphy Hospital (1922-1930); member of the visiting staff, St. Louis City Hospital (1917-1924); otolaryngologist, St. Louis County Hospital (1932-1935); and at the time of his death; associate otolaryngologist, St. Louis City Hospital; assistant otolaryngologist, St. Mary's Group of Hospitals; associate otolaryngologist, Bethesda Hospital; otolaryngologist, St. Luke's Hospital; otolaryngologist, De Paul Hospital; otolaryngologist, Deaconess Hospital; and otolaryngologist, Jewish Hospital.

Doctor Wood was a member of the St. Louis Medical Society, Missouri State Medical Association, the American Medical Association, the St. Louis Clinics, the St. Louis Ear, Nose and Throat Club, the American Academy of Ophthalmology and Otolaryngology, the American Laryngological, Rhinological and Otological Society, and a fellow of the American College of Surgeons, the American Laryngological Association and the American Otological Society.

He married Helen Isabel Adkins of St. Louis, Mo., in 1918, and this union was blessed with three children. His philanthropic inter-

ests were confined to the United Charities of St. Louis, the Zoological Society of St. Louis and the Tuberculosis Society of St. Louis. He was a member of the Glen Echo Country Club and his main diversions were golf and bridge.

Doctor Wood was a consistent but not profuse contributor to the literature of his specialty. He spoke and wrote only when he felt he had a worth while message to convey. His articles were based upon a broad clinical experience and reflected complete honesty in their interpretation. As a teacher he was patient, thorough and sympathetic.

Executive Sessions

1949

FIRST EXECUTIVE SESSION

MAY 16, 1949

The First Executive Session of the American Laryngological Association held in connection with the Seventieth Annual Meeting at the Hotel Biltmore, New York City, convened at 12:30 noon, following the first scientific session. Dr. Frederick T. Hill, President of the Association, presided.

On recommendation of the Council the following were elected to *Honorary Fellowship:*

DR. GEORGE M. COATES

To Emeritus Fellowship:

DR. CHARLES J. IMPERATORI

To Active Fellowship:

DR. AUGUST L. BECK, New Rochelle, New York

DR. JOHN R. LINDSAY, Chicago, Ill.

The DeRhoaldes Award was presented to Dr. George M. Coates.

The Newcomb Award for 1949 was given to Dr. Gordon B. New.

The Association elected the following to serve as a Nominating Committee:

DR. GORDON BERRY

DR. H. MARSHALL TAYLOR

DR. J. MACKENZIE BROWN

DR. ARTHUR W. PROETZ

DR. HAROLD I. LILLIE

DR. HARRIS P. MOSHER (honorary)

There being no further business the session adjourned at 12:50 P. M.

Respectfully submitted,

LOUIS H. CLERF,

Secretary.

ANNUAL BUSINESS MEETING

May 17, 1949

The Annual Business Meeting, the second Executive Session of the American Laryngological Association was called to order at 12:05 noon, following the close of the Scientific Session by President Hill.

Report of the Secretary was accepted and filed.

Report of the Treasurer was accepted and filed.

The Nominating Committee recommended the following Fellows to serve as Board of Directors of the Association for the year 1949-1950:

Dr. Ralph A. Fenton
Dr. Leroy A. Schall
Dr. Fletcher D. Woodward
Dr. Louis H. Clerf
Dr. Gordon F. Harkness
Dr. Harry P. Schenck
Dr. Harold I. Lillie
Dr. Francis E. LeJeune
Dr. Arthur W. Proetz
Dr. Frederick T. Hill

The report of the Nominating Committee was accepted unanimously.

The Biographer and Historian, Dr. Harry P. Schenck reported the names of the following Fellows whose death occurred since the last meeting of the Association:

Active Fellows:

V. Visscher Wood

Corresponding Fellows:

James F. McKernon
Lionel Colledge
Ernst Schmiegelow

Emeritus Fellows:

SECORD HERBERT LARGE
SAMUEL MCCULLAGH
JOHN B. POTTS
J. GORDON WILSON

The Membership rose and stood in silence in honor of the departed Fellows.

Dr. A. W. Proetz reporting for the American Board of Otolaryngology stated that the examination was held in New York City, N. Y. on May 11th to 13th, 1949. Eighty-four candidates were examined, 56 were passed.

The Secretary reporting for the Casselberry Award Committee indicated that the Casselberry Award for 1949 had been awarded to Dr. Harry B. Orton. Newark, N. J. for his thesis entitled "Laryngectomies and Laryngopharyngectomies." The report was accepted and filed.

The report of the Memorial Fund Committee was presented. This was accepted and filed.

The Special Committee appointed by Council to draw up a resolution relative to the present controversial compulsory health insurance plan presented its report.

It was regularly moved, seconded and passed that the Resolution be approved and that a copy be sent to the American Medical Association.

The Executive Session adjourned at 12:40 P. M.

LOUIS H. CLERF,
Secrtary.

REPORT OF THE SECRETARY
AMERICAN LARYNGOLOGICAL ASSOCIATION
MAY 15, 1949

The Sixty-Ninth Annual Meeting of the American Laryngological Association was held on April 14 and 15, at The Homestead, Hot Springs, Va., under the Presidency of Dr. Arthur W. Proetz. Sixty-two fellows and fifty-three guests were in attendance.

Fifteen scientific papers were well received. The hotel and meeting facilities were very satisfactory.

The following were elected:

To Emeritus Fellowship:

DR. JOHN L. MYERS, Kansas City, Mo.
DR. FRANK R. SPENCER, Boulder, Colo.

To Active Fellowship:

DR. JAMES H. MAXWELL, Ann Arbor, Mich.
DR. KENNETH A. PHELPS, Minneapolis, Minn.
DR. EDWARD J. WHALEN, Hartford, Conn.
DR. HENRY L. WILLIAMS, 2ND, Rochester, Minn.

The Newcomb Award for 1948 was given to Dr. Gordon Berry.

The following Officers were elected:

President	Frederick T. Hill, M.D.
First Vice-President	Henry B. Orton, M.D.
Second Vice-President	Anderson C. Hilding, M.D.
Secretary	Louis H. Clerf, M.D.
Treasurer	Gordon F. Harkness, M.D.
Librarian and Historian	Harry P. Schenck, M.D.
First Councillor	Charles J. Imperatori, M.D.
Second Councillor	Harold I. Lillie, M.D.
Third Councillor	Francis E. LeJeune, M.D.
Fourth Councillor	Arthur W. Proetz, M.D.

The Association has lost through death in the past year 4 Emeritus Fellows 1 Corresponding Fellow and 1 Active Fellow.

The membership as of this date is

Active	94
Honorary	4
Corresponding	12
Emeritus	14
Total	124

The Council at its Annual Meeting in January 1949 recommended

For Honorary Fellowship:

GEORGE M. COATES, M.D.

For Emeritis Fellowship:

CHARLES J. IMPERATORI, M.D.

For Active Membership:

AUGUST BECK, M.D., New Rochelle, N. Y.

JOHN LINDSAY, M.D., Chicago, Ill.

Dr. Samuel Salinger was reappointed Abstract Editor.

The Council approved a registration fee of $12.00 for Fellows for the Annual Meeting.

The Council designated Dr. Bernard J. McMahon as Chairman and Dr. Francis E. LeJeune as the new member of the Memorial Fund Committee to be elected at the annual meeting in 1949.

Publication of the Transactions can be expedited if blocks for illustrations are secured promptly. Essayists are requested to send to the Secretary the name of the medical Journal which will publish their paper so that blocks may be obtained.

Respectfully submitted,

LOUIS H. CLERF,

Secretary.

REPORT OF THE TREASURER AND AUDITORS

Balance Sheet

April 1, 1949

ASSETS

General Fund:		
Checking Account	$3,962.11	
Less: Due Trust Fund	2,787.88	
Total General Fund Assets		$ 1,174.23
Trust Funds:		
Savings Account	$2,766.54	
Add: Due From General Fund—Above	2,787.88	
Total Trust Fund Cash		$ 5,554.42

Bonds:

	Par	Cost
U. S. Defense 2½—G—1953	$3,000.00	3,000.00
U. S. Defense 2½—G—1954	1,000.00	1,000.00
U. S. Treasury 2¼—1956/59	1,000.00	1,003.50
U. S. Defense 2½—7—1956	5,000.00	5,000.00
U. S. Defense 2½—G—1957	1,000.00	1,000.00
U. S. Defense 2½—G—1958	2,000.00	2,000.00
U. S. Treasury 2¾—1858/63	1,000.00	1,101.20
U. S. Treasury 2½—1964/69	3,000.00	3,000.00
U. S. Treasury 2½—1967-72	1,000.00	1,000.00
U. S. Savings 2½—G—1959	5,000.00	5,000.00
U. S. Savings 2½—G—1960	1,000.00	1,000.00
U. S. Savings 2½—G—1961	1,000.00	1,000.00

Total Bonds—At Cost		$25,104.70
Total Trust Funds Assets		$30,659.12
Total Assets		$31,833.35

LIABILITIES AND NET WORTH

General Fund:		
Capital and Surplus:		
Balance April 1, 1948	$929.65	
Add: Excess of Receipts over Disbursements for the Year Ended April 1, 1949	244.58	
Balance April 1, 1949—General Fund		$ 1,174.23

Trust Funds:

Fund	Principal	Unused Income April 1, 4918	Expended 1948-49	Income 1948-49	Unsued Income April 1, 1949	Principle and Unused Income April 1, 1949
Casselberry	$ 5,000.00	$ 379.59	$	$109.99	$ 489.58	$ 5,489.58
Johnston	5,000.00	322.82		108.88	431.70	5,431.70
deRoaldes	3,095.00	39.04		63.76	102.80	3,197.80
Newcomb Trust	2,000.00	299.24	98.10	45.06	246.20	2,246.20
Newcomb Prize	500.00	2.82	4.00	10.12	3.30	503.30
Hourn Scolarship	1,000.00			20.23	20.23	1,020.23
Memorial	11,564.19	951.07		255.05	1,206.12	12,770.31
Totals	$28,159.19	$1,988.94	$102.10	$613.09	$2,499.93	$30,659.12
Total Liabilities and Net Worth						$31,833.35

STATEMENT OF INCOME AND EXPENSE ALL FUNDS FOR THE YEAR ENDED APRIL 1, 1949

Income:		
Dues		$3,550.00
Registration Fees		580.00
Sale of Transactions		152.50
Income—Trust Funds Interest		666.01
Total Income		$4,948.51
Expenditures:		
Expenditures Charged to the Association:		
Annual Meeting:		
Dinner-Cocktail Party	$288.28	
Council Session	19.70	
Projection Service	50.00	
Printing	166.90	
Reporting Service	129.16	$ 654.04
Officers' Clerical Hire		500.00
Transactions Expense		1,929.01
Council Meeting		498.29
Stationery and Printing		280.58
Postage		6.00
Treasurer's Bond		75.00
Transferred to deRhoaldes Fund		95.00
Total Expenditures Charged to the Association		$4,037.92
Expenditures Charged to Trust Funds:		
Closing Old Bank Account		$ 2.10
Transportation—Archives		3.00
Delavan Collection Work (Dr. Imperatori)		93.00
Engrossing Newcomb Award		4.00
Total Expenditures Charged to Trust Funds		$ 102.10

Allocation of Income—Trust Funds:			
Loss on Bond Called	$101.20		
Less: Loss Absorbed by Reserve for Losses on Investments	48.28		
Loss Charged to Trust Funds—Unused Income		$ 52.92	
Balance of Income—Trust Funds, Allocated to Trust Funds—Unused Income		613.09	
Total Allocated			666.01
Total Expenditures			$4,806.03
Excess of Income over Expenditures			$ 142.48
Add: Expenditures Charged to Trust Fund (Above)			102.10
Net Excess of General Fund Income over Expenditures—To General Capital and Surplus			$ 244.58

STATEMENT OF INCOME AND EXPENSE—GENERAL FUND

FOR THE YEAR ENDED APRIL 1, 1949

Income:			
Dues		$3,550.00	
Registration Fees		580.00	
Sale of Transactions		152.50	
Total Income			$4,282.50
Expenditures:			
Annual Meeting:			
Dinner-Cocktail Party	$288.28		
Council Session	19.70		
Projection Service	50.00		
Printing	166.90		
Reporting Service	129.16	$ 654.04	
Officers' Clerical Hire		500.00	
Transactions Expense		1,929.01	
Council Meeting		498.29	
Stationery and Printing		280.58	
Postage		6.00	
Treasurer's Bond		75.00	
Transferred to deRhoaldes Fund		95.00	
Total Expenditures			$4,037.92
Excess of Income Over Expenditures—General Fund			$ 244.58

STATEMENT OF INCOME AND EXPENSE—TRUST FUNDS FOR THE YEAR ENDED APRIL 1, 1949

Income—Trust Fund Interest		$ 666.01
Loss on Investments:		
Loss on Bond Called	$ 101.20	
Less Loss Absorbed by Reserve for Losses on Investments Provided in Prior Years	48.28	
Net Loss on Investments to be Charged Against Income		$ 52.92
Net Income To Be Allocated to Trust Funds		$ 613.09
Expenditures Chargeable to Particular Trust Funds:		
Closing Old Bank Account	$ 2.10	
Transportation — Archives	3.00	
Delavan Collection Work (Dr. Imperatori)	93.00	
Engrossing Newcomb Award	4.00	
Total Expenditures		$ 102.10
Net Increase in Unused Income—Trust Funds		$ 510.99

SECURITY AND FUND TRANSACTIONS FOR THE YEAR ENDED APRIL 1, 1949

Security Transactions:

Purchased:

$1,000.00 U. S. Savings Bond Series "G" 2½ 1961 ..... $1,000.00

Called:

$1,000.00 U. S. Treasury Bond 2¾% 1948/51

Purchase Price	$1,101.20	
Call Price	1,000.00	
Net Loss on Transaction		$ 101.20

Fund Transactions:

Principal of Trust and Scholarship Funds—April 1, 1948		$27,004.19
Contributions Received During the Year:		
Memorial Fund:		
Dr. H. Marshall Taylor	$100.00	
Dr. W. W. Eagle	100.00	
Dr. F. Z. Havens	100.00	
Dr. L. Clerf	350.00	
Dr. F. W. Dixon	25.00	
Dr. G. F. Harkness	100.00	
Dr. T. C. Galloway	10.00	
Dr. H. P. Holinger	25.00	$ 810.00

George E. Hourn Scholarship:		
Dr. George E. Hourn	250.00	
Total Contributions	$1,060.00	
Transfer to deRhoaldes Fund from General Fund	95.00	
Total Additions to Principal of Funds		1,155.00
Principal of Trust and Scholarship Funds—April 1, 1949		$28,159.19

Respectively submitted,

GORDON F. HARKNESS,

Treasurer.

April 1, 1949.

ACCOUNTANTS' REPORT

We have examined the balance sheet of American Laryngological Association as of April 1, 1949, and the related statement of income and expense for the year then ended. Our Examination was made in accordance with generally accepted auditing standards and, accordingly, included such tests of the accounting records and such other auditing procedures as we considered necessary in the circumstances, with the exception that fund balances were accepted as shown by the books without independent verification by us.

ACCOUNTANT'S OPINION

In our opinion, the accompanying balance sheet and statement of income and expense present fairly on a cash receipts and disbursements basis the financial position of American Laryngological Association at April 1, 1949, and the results of its operations for the year then ended, in conformity with generally accepted accounting principles applied on a basis consistent with that of the preceding year.

Respectfully submitted,

McGladrey, Hansen, Dunn & Co.

1948-1949 REPORT OF THE MEMORIAL FUND COMMITTEE

MAY 12, 1949

Gifts from seven men totalling $1,300 were reported last year. During 1948-1949, there have been nine gifts totalling $810 from Drs. Berry, Clerf, Dixon, Eagle, Galloway, Harkness, Havens, Holinger, and Taylor. Last month after the 1949 books were closed, Dr. Johnston sent in the first of a series of annual checks, which will appear in next year's report.

The Benefactors up to date and given in chronological order are: Drs. Barnhill, Dean (by his wife), Berry, Hill, Hourn (by his wife), Salinger, and Taylor. This year the Committee recommends that we add to this list (of those who have given $500 or more) the name of Dr. Louis H. Clerf.

The principal sum in this Fund is now $11,564.19 and the accumulated income available to be spent is $1,206.12. An annual income of $255.05 comes from the principal fund. (This includes $250 from the Hourn Fund.) To be added to these are promised bequests from Mrs. George Fetterholf Kennedy, $5,000 (1936 Trans.), from Mrs. George E. Hourn, $10,000 (1946 Trans.) and from two anonymous donors, $10,000 (1941 Trans.) and $1,000 (1943 Trans.) making an expected total to date of $37,664.19. In addition, others have signified their intention to make bequests, and this year one fellow informs me he is bequeathing the bulk of his considerable estate to this Fund.

Though the annual income is still small, it is now sufficient to help some promising laryngologist in constructive research. Each Fellow is asked to bear this in mind as some able young laryngologist comes to his attention. Please contact Dr. Clerf or a member of the Committee about him.

The Rules governing this Memorial Fund appear on page 488 of the 1940 Transactions. We venture the opinion that the agency thus established is the safest, wisest and the most permanent one available for consistent and continuing laryngologist research. To foster interest and support, an informative letter was sent to each Fellow last March.

The Council has informed us that it proposes for your ratification, Dr. McMahon as Chairman of this Committee and Dr. LeJeune as the new member to succeed Dr. Berry.

It is hereby moved:

1. That Dr. Bernard J. McMahon be appointed as Chairman for the ensuing year and Dr. Francis E. LeJeune as the 1949 to 1954 member of this Committee.

2. That Dr. Louis H. Clerf be declared a Benefactor of this Fund and that his name be so recorded in our Transactions.

3. That this report be accepted and entered in the Transactions.

Respectfully submitted,

GORDON BERRY, *Chairman* '49
BERNARD J. MCMAHON '50
OLIVER E. VANALYEA '51
FLETCHER E. WOODWARD '52
H. MARSHALL TAYLOR '53

REPORT OF REPRESENTATIVES ON AMERICAN BOARD OTOLARYNGOLOGY

Your representatives to the American Board of Otolaryngology have the honor to report that at an examination held last week in New York City 84 candidates were examined of whom 56 will receive certificates. An examination will be held in October 1949 in Chicago, and to accommodate the demand, there will be an extra examination in January 1950 at a place still to be designated.

A copy of of the new requirements becoming effective in 1950 has been filed with the Secretary.

Respectfully submitted,

ARTHUR W. PROETZ,
FREDERICK T. HILL.

REPORT OF SPECIAL COMMITTEE ON RESOLUTIONS

Be it resolved by the American Laryngological Association assembled in its seventieth Annual Meeting that first—It reaffirms its fast accepted policy of a willingness to cooperate in Health Legislative Programs to improve the medical care and decrease economic burdens of the same for the people of the United States. Secondly—that it is opposed to the so called Truman Compulsory Health and Insurance Program as embodied in Senate Bill No. ---------- and House File No. ---------- for the following reasons.

1. The medical care for the people of the United States will, as exemplified in other countries, deteriorate under such a system.

2. The actual cost of medical service as advocated will mean a staggering increase, no small part of which will be the administrative costs, by an enormous federal bureau, which will operate not on a budget, but with the aid of hidden taxes, reflected in higher living costs.

3. Governmental Compulsory Health Insurance is essentially Socialized Medical Care. This is confirmed by the experience of other nations who have tried it. It has been the opening wedge of dictators and advocates of a socialized form of government. Of fundamental importance is the fact that such a program strikes at the cornerstone of our democracy; it is a part of governmental regimentation, as opposed to the system of free enterprise and the rights of citizenship thru which our country has continued to advance from its very beginning.

Be it further resolved that the Secretary of the American Laryngological Association transmit these resolutions to those members of Congress having an active interest in the above proposed legislation.

HENRY B. ORTON, *Chairman,*

HARRY P. SCHENCK,

GORDON F. HARKNESS.

FINAL EXECUTIVE SESSION

MAY 17, 1949

The final Executive Session was called to order by President Hill on Tuesday, May 17, 1949 at 4:25 P. M. On motion from the floor the report of the Nominating Committee was presented and unanimously accepted. The meeting recessed while the new Board of Directors retired and elected the following Officers for the ensuing year:

President	Dr. Ralph A. Fenton
First Vice-President	Dr. Leroy A. Schall
Second Vice-President	Dr. Fletcher D. Woodward
Secretary	Dr. Louis H. Clerf
Treasurer	Dr. Gordon F. Harkness
Librarian and Historian	Dr. Harry P. Schenck
First Councilor	Dr. Harold I. Lillie
Second Councilor	Dr. Frances E. LeJeune
Third Councilor	Dr. Arthur W. Proetz
Fourth Councilor	Dr. Frederick T. Hill

The President-Elect Dr. Ralph A. Fenton was conducted to the Rostrum and delivered a brief address of acceptance.

There being no further business the meeting adjourned sine die.

Respectfully submitted,

LOUIS H. CLERF,

Secretary.

List of Fellows

1949

LIST OF FELLOWS

Date Indicates Year Admitted to Active Fellowship

Attendance at meetings is shown by figures following each name.
Asterisk (*) indicates year paper was read.

Active Fellows

1942. Ashley, Rea E., 384 Post Street, San Francisco 8, California, 1946, '47, '48, '49.

1936. Ballenger, Howard C., 723 Elm Street, Winnetka, Illinois, 1936, '37, '38*, '40, '41, '42, '46*, '47, '48.

1944. Beatty, Hugh G., 150 East Broad Street, Columbus 15, Ohio, 1944, '46*, 47, '48, '49.

1949. Beck, August Leo, 42 Hugenot Street, New Rochelle, N. Y., 1949.

1921. Berry, Gordon, 36 Pleasant Street, Worcester, Massachusetts, 1921*, '22, '23, '24, '25, '26, '27, '28*, '29*, '30, '31, '32, '33, '34, '35, '37, '38, '39, '40, '41*, '42, '44, '46, '47, '48, '49.

1938. Blassingame, Charles Decatur, 414 P. and S. Building, Memphis 3, Tennessee, 1938, '39, '41, '42, '44, '46*, '47.

1944. Boies, Lawrence R., 1631 Medical Arts Building, Minneapolis 2, Minnesota, 1944, '46, '47, '48*, '49.

1941. Bowers, Wesley C., 17 East 61st Street, New York 21, N. Y., 1941, '42, '44, '49.

1932. Brown, John Mackenzie, 1136 W. 6th Street, Los Angeles, 14, California, 1935*, '37, '40*, '41, '42, '44, '47*, '49.

1940. Broyles, Edwin N., 1100 North Charles Street, Baltimore, Maryland, 1940, '41*, '42*, '46, '47, '48*, '49.

1930. Campbell, Edward Hastings, Spruce Street Medical Bldg., 19th and Spruce Streets, Philadelphia 3, Pennsylvania, 1930, '31*, '32*, '33, '35, '38, '39*, '40, '41, '47, '48, '49.

1945. Campbell, Paul A., 700 North Michigan Avenue, Suite 314, Chicago, Illinois, 1946, '47, '49.

1942. CANFIELD, NORTON, 789 Howard Avenue, New Haven, Connecticut, 1942, '46, '47, '48, '49*.

1925. CLERF, LOUIS H., 1530 Locust Street, Philadelphia 2, Pennsylvania, 1925, '27*, '28, '29*, 30*, '32, '33, '34, '35, '36*, '37, '38, '39, '40, '41*, '42*, '44*, '46, '47, '48, '49.

1939. CODY, CLAUDE CARR, 1304 Walker Avenue, Houston, Texas, 1939, '41, '42, '44, '46*, '47, '48*, '49.

1937. CROWE, SAMUEL JAMES, 4332 North Charles Street, Baltimore, 18, Maryland, 1937, '38*, '40, '42, '44*, '48*.

1941. CUNNING, DANIEL S., 121 East 60th Street, New York 22, N. Y., 1941, '42*, '44, '46, '47*, '48, '49.

1941. DIXON, FRED W., 1027 Rose Building, Cleveland, Ohio, 1941, '42*, '44, '46, '47*, '49*.

1947. EAGLE, WATT WEEMS, Duke Hospital, Durham, N. C., 1948*, '49.

1947. ENGLER, CLARENCE W., 2323 Prospect Avenue, Cleveland, Ohio, 1947, '48*, '49.

1923. FENTON, RALPH ALBERT, 1020 S.W. Taylor Street, Portland 5, Oregon, 1923, '25*, '26, '28, '30, '32, '34, '35, '37*, '39, '40*, '42, '44, '46, '47*, '49.

1930. FIGI, FREDERICK A., Mayo Clinic, Rochester, Minnesota, 1930, '32*, '34, '35, '38*, '42*, '47*, '48.

1932. FURSTENBERG, ALBERT CARL, 201 South Main Street, Ann Arbor, Michigan, 1933*, '36*, '38*, '46, '47, '48*.

1936. GALLOWAY, THOMAS CYRUS, 636 Church Street, Evanston, Illinois, 1936, '37, '38*, '39, '40, '41, '42*, '46*, '47, '48.

1940. GATEWOOD, E. TRIBLE, Professional Building, Richmond, Virginia, 1940, '41, '42*, '44, '47.

1940. GILL, WILLIAM D., 705 East Houston Street, San Antonio, Texas, 1940, '41*, '46.

1928. GITTINS, THOMAS ROY, 408 Davidson Building, Sioux City, Iowa, 1928, '31, '32*, '34, '36, '39*, '40, '42*, '47.

1940. GOODALE, ROBERT L., 330 Dartmouth Street, Boston, Massachusetts, 1940, '41, '42*, '44*, '46, '47, '49.

1928. Goodyear, Henry M., 556 Doctors' Building, Cincinnati 2, Ohio, 1928, '29, '30*, '31, '32, '33, '34*, '35, '36, '37, '38, '39, '40, '42, '44*, '46, '47, '48, '49*.

1934. Grove, William E., 324 East Wisconsin Avenue, Milwaukee, 2, Wisconsin, 1934, '35, '36*, '37, '38, '39, '40, '41, '42*, '44, '46, '47, '48, '49.

1940. Hansel, French K., 634 North Grand Avenue, St. Louis 3, Missouri, 1940, '42, '46, '47.

1933. Harkness, Gordon Follette, 2410 River Drive, Davenport, Iowa, 1934, '35, '36*, '40, '41, '44, '46, '47, '48, '49.

1944. Havens, Fred Z., 102 Second Avenue S-W., Rochester, Minnesota, 1944, '46, '49.

1942. Heatley, Clyde A., 11 North Goodman Street, Rochester, N. Y., 1942, '46*, '49.

1945. Hickey, Harold L., 1612 Tremont Street, Denver 2, Colorado, 1946, '47, '48, '49.

1943. Hilding, Anderson C., 324 West Superior Street, Duluth, Minnesota, 1944*, '46, '47, '48*, '49.

1928. Hill, Frederick Thayer, Professional Building, Waterville, Maine, 1928, '29*, '30*, '31, '32, '33, '34, '35, '36, '37*, '38*, '39, '40, '41*, '42, '44*, '46, '47, '48, '49*.

1945. Holinger, Paul H., 700 North Michigan Ave., Chicago 11, Illinois, 1946, '47, '49.

1944. Hoople, Gordon D., Medical Building, Syracuse, New York, 1946, '47, '48, '49.

1930. Houser, Karl Musser, 2035 Delancey Street, Philadelphia 3, Pennsylvania, 1930, '32*, '33, '34*, '37, '38, '39, '40, '41, '44, '48.

1939. Hunt, Westley Marshall, 907 Fifth Avenue, New York 21, N. Y., 1939, '40*, '41, '42, '44, '46, '47, '48, '49.

1938. Jackson, Chevalier Lawrence, Temple University Hospital, Philadelphia 40, Pa., 1938, '39, '40, '41*, '42, '44*, '46, '47*, '48, '49.

1928. JARVIS, DEFOREST CLINTON, Quarry Bank Building, Barre, Vermont, 1928, '30, '32*, '33, '34*, '35, '37*, '38, '39, '40, '41, '44, '46, '47, '48, '49.

1939. JOHNSTON, WILLIAM HOWARD, 1515 State Street, Santa Barbara 7, California, 1939, 40, '41, '42, '44, '46, '47, '49.

1944. JONES MARVIN F., 121 E. 60th Street, New York City, 1944, '46, '47, '48, '49.

1942. KELLY, JOSEPH D., 140 East Fifty-fourth Street, New York 22, N. Y., 1942, '44*, '47, '48, '49.

1921. KERNAN, JOHN D., JR., 103 East Seventy-eighth Street, New York City 21, 1921*, '22, '25, '26, '27, '29, '31, '34*, '35, '36, '37*, '39, '40*, '42*, '47, '48.

1942. KING, EDWARD D., 6777 Hollywood Blvd., Hollywood 28, California, 1942, 46, '47, '49*.

1936. LEJEUNE, FRANCIS ERNEST, Ochsner Clinic Building, Prytania and Aline Streets, New Orleans, Louisiana, 1937, '46*, '47.

1933. LIERLE, DEAN M., University Hospital, Iowa City, Iowa, 1933, '34, '35*, '37, '38, '39, '40*, '42*, '44*, '46, '47*, '48, '49.

1922. LILLIE, HAROLD I., Mayo Clinic, Rochester, Minnesota, 1923*, '24*, '25, '26*, '28, '31*, '33, '36*, '37, '38, '40, '44, '46*, '47, '48*, '49*.

1949. LINDSAY, JOHN R., 950 E. 59th St., Chicago 37, Ill., '49.

1935. LOOPER, EDWARD A., 104 West Madison Avenue, Baltimore 1, Maryland, 1935, '36, '37, '38*, '39, '41, '42, '44, '47, '48*, '49.

1927. LUKENS, ROBERT M., 1308 Hunting Park Avenue, Philadelphia 40, Pennsylvania, 1927, '28, '31*, '32, '35, '36, '38, '39, '40*, '42, '46, '48*, '49.

1939. LUPTON, IRVING MARTIN, 806 Medical Arts Building, Portland, Oregon, 1946.

1929. LYMAN, HARRY WEBSTER, 906 Carleton Building, St. Louis 1, Missouri, 1929, '31, '34, 35*, '36, '38, '39, '42, '44, '46, '47, '48, '49.

1928. MACPHERSON, DUNCAN, 920 Fifth Avenue, New York City 21, 1928, '29, '30, '31, '33, '34*, '39, '40, '41, '44, '49.

1941. MARTIN, ROBERT C., 384 Post Street, San Francisco 8, California, 1941, '44, '47, '48.

1948. MAXWELL, JAMES H., 201 S. Main Street, Ann Arbor, Michigan, 1948, '49.

1939. MCCASKEY, CARL HEBER, 608 Guaranty Building, Indianapolis 4, Indiana, 1939, '40, '41, '42*, '44, '46*, '47, '48, '49.

1945. MCLAURIN, JOHN G., 1322 Medical Arts Building, Dallas 1, Texas, 1946, '49.

1933. MCMAHON, BERNARD J., Missouri Theatre Building, St. Louis 3, Missouri, 1934*, '35, '36, '38*, '41, '44, '46*, '47, '48, '49.

1931. MCNALLY, WILLIAM JAMES, 1509 Sherbrooke Street West, Montreal, Canada, 1931, '33, '34*, '39, '44, '47, '48, '49.

1940. MORRISON, WILLIAM W., 140 E. 54th Street, New York 22, N. Y., 1940, '41*, '44, '47, '49*.

1927. MYERSON, MERVIN C., 416 North Bedford Drive, Beverly Hills, California, 1927, '28*, '29, '30, '31*, '32*, '33*, '34*, '35, '36, '37, '38, '39*, '40, '41*, '42, '44.

1937. NASH, C. STEWART, Medical Arts Building, Rochester 7, New York, 1937, '38*, '40, '42, '44, '46, '47, '49.

1922. NEW, GORDON B., Mayo Clinic, Rochester, Minnesota, 1922, '24, '25*, '26*, '28*, '31*, '33*, '35*, '37*, '39*, '41*, '46*, '48*, '49*.

1927. ORTON, HENRY BOYLAN, 224 Delavan Avenue, Newark 4, New Jersey, 1927, '28, '29, '30*, '31, '32, '33*, '35, '36, '37, '38*, '40, '41, '42, '44*, '46, '47*, '49.

1948. PHELPS, KENNETH A., 1137 Medical Arts Building, Minneapolis 2, Minnesota, 1948.

1924. PROETZ, ARTHUR WALTER, 1010 Beaumont Building, St. Louis 3, Missouri, 1924, '25*, '26*, '27, '28, '29, '30, '31, '32*, '33*, '34, '35*, '36, '37, '38*, '39*, '40, '41, '42*, '44, '46, '47*, '48*, '49*.

1934. RICHARDS, LYMAN GILDER, 520 Commonwealth Avenue, Boston, Massachusetts, 1934, '35, '36*, '37, '38, '39, '47, '49.

1930. RIDPATH, ROBERT F., 1720 Spruce Street, Philadelphia 3, Pennsylvania, 1930, '31, '33, '37, '38*, '40, '41*, '44, '47, '49.

1945. ROBB, JAMES M., 641 David Whitney Building, Detroit, Michigan, 1946, '48, '49*.

1938. SALINGER, SAMUEL, 25 E. Washington Street, Chicago, Illinois, 1938, '39, '40*, '42, '44*, '46, '47, '48, '49.

1921. SAUER, WILLIAM E., 3720 Washington Boulevard, St. Louis 8, Missouri, 1921, '23, '25, '28, '31, '32, '35, '37, '39*, '41, '44, '47.

1932. SCHALL, LEROY ALLEN, 243 Charles Street, Boston 14, Massachusetts, 1934*, '35, '38, '40*, '41, '42, '44*, '46, '47, '48*, '49.

1934. SCHENCK, HARRY P., 326 South 19th Street, Philadelphia 3, Pennsylvania, 1934, '35, '36*, '37, '38, '39, '40, '41*, '44*, '46, '47, '49.

1930. SEYDELL, ERNEST M., First National Bank Building, Wichita, Kansas, 1930, '31*, '33*, '34, '35, '37*, '38, '39, '40*, '41, '42, '46, '47, '48.

1928. SHEA, JOHN JOSEPH, 1018 Madison Avenue, Memphis, Tennessee, 1928, '29, '30*, '31, '32*, '33, '34, '35, '36, '37, '38, '40. '41*, '42, '46, '47*, '48, '49.

1909. SHURLY, BURT R., 62 Adams Avenue W., Detroit, Michigan, 1920, '21*, '22, '24, '25*, '26, '27*, '28, '29*, '30, '31, '33, '34, '35, '36, '37, '38, '39, '40, '41, '42, '44, '46, '47, '48, '49.

1939. SIMPSON, W. LIKELY, 512 Physicians' and Surgeons' Building, Memphis 3, Tennessee, 1939, '41, '44*, '46, '47*, '48.

1924. TAYLOR, HERMON MARSHALL, 111 West Adams Street, Jacksonville 5, Florida, 1924, '25*, '26, '27, '28, '31, '34, '35*, '36, '37, '38, '39*, '40, '41 ,'42, '44*, '46, '47, '48, '49.

1947. THEOBALD, WALTER H., 307 N. Michigan Avenue, Chicago, Illinois, 1947, '48*, '49.

1927. TOBEY, HAROLD G., 403 Commonwealth Avenue, Boston 15, Massachusetts, 1927, '29*, '30*, '31, '32, '35, '37, '39, '41, '46, '48, '49.

1925. TUCKER, GABRIEL, 250 South Eighteenth Street, Philadelphia, 3, Pennsylvania, 1925, '26*, '27*, '29, '30, '31, '32, '33, '34, '35*, '36, '37, '38, '39, '40*, '41*, '42, '46, '47, '48, '49.

1943. VAN ALYEA, OLIVER E., 135 South LaSalle Street, Chicago, Illinois, 1944, '46*, '47, '48, '49.

1941. VIOLE, PIERRE P., 1930 Wilshire Boulevard, Los Angeles 5, California, 1944*, '46, '47.

1940. WEILLE, FRANCIS L., 247 Commonwealth Avenue, Boston 16, Massachusetts, 1940, '41, '42, '44, '46*, '47, '48, '49.

1948. WHALEN, EDWARD J., 750 Main Street, Hartford, Connecticut, 1948.

1922. WHITE, FRANCIS W., 471 Park Avenue, New York 22, N. Y., 1922, '23*, '25, '26, '27, '28, '29, '31, '32, '37, '39, '40, '41, '42, '44, '46*, '49.

1948. WILLIAMS, HENRY L. 2nd, Mayo Clinic, Rochester, Minnesota, 1948, '49*.

1939. WILLIAMS, HORACE JAMES, 5908 Greene Street, Germantown, Philadelphia, 1939, '40, '41, '42, '46, '47*, '49.

1942. WISHART, D. E. STAUNTON, 170 St. George Street, Toronto, Canada, 1942, '44, '46, '47*, '49.

1935. WOODWARD, FLETCHER D., 104 East Market Street, Charlottesville, Virginia, 1935, '36*, '37, '38, '39*, '40, '42, '44, '47, '48, '49.

Honorary Fellows

1949. (1917) COATES, GEORGE M., 1721 Pine Street, Philadelphia 3, Pa., 1949*.

1939. (1907) JACKSON, CHEVALIER, Schwenksville, Pennsylvania, 1939*, '40*.

1943. (1918) LEWIS, FIELDING O., Providence Road, Media, Pennsylvania.

1947. (1904) MOSHER, HARRIS P., 127 Front Street, Marblehead, Mass., 1947, '48, '49.

1937. NAGER, F. B., Freiestrasse 3, Zurich, Switzerland.

Corresponding Fellows

1946. Alonso, Justo M., Mercedes 1233, Montevideo, Uruguay.

1942. Batson, Oscar V., 133 South Thirty-sixth Street, Philadelphia 4, Pennsylvania, 1942*.

1938. Blair, Vilray P., 508 North Grand Avenue, St. Louis 3, Missouri.

1943. Eggston, Andrew O., 653 Park Avenue, New York, N. Y., 1944, '49.

1921. Le Maitre, Fernand, Avenue Victor Hugo, 120 (XVI), Paris, France.

1930. Negus, Victor E., 149 Harley Street, London, W 1, England, 1938*.

1941. Patterson, Norman, Nobs Creek, Ashbridge Park, Berkhamsted, Herts, England.

1937. Portmann, Georges, 25 bis Cours de Verdun, Bordeaux, France, 1947.

1924. Schaefer, J. Parsons, Jefferson Medical College, Philadelphia, Pennsylvania, 1934.

1936. Vialle, Jacques, 27 Rue de France, Nice (Alpes Maritimes), France.

Emeritus Fellows

1941. (1923) Barlow, Roy A., Medical Arts Building, Winchester, Virginia.

1937. (1915) Barnes, Harry Aldrich, Kingston, Mass., R.F.D. No. 2.

1944. (1913) Butler, Ralph, 1930 Chestnut Street, Philadelphia, Pennsylvania.

1946. (1933) Foster, John H., Eagle Lake, Texas, 1948, '49.

1941. (1922) Goldsmith, Perry G., 513 Medical Arts Building, Toronto, Canada, 1949.

1936. (1898) Goodale, Joseph L., Argilla Road, Ipswich, Massachusetts.

1943. (1932) GRAHAM, HARRINGTON B., Bohemian Club, San Francisco 2, California.

1940. (1917) GREENE, JOSEPH B., 336 Vanderbilt Road, Asheville, North Carolina.

1933. (1905) HALSTED, THOMAS H., 40 Trinity Place, Boston 16, Mass., 1949.

1949. (1920) IMPERATORI, CHARLES J., Block House, Essex, N. Y., 1949.

1948. (1939) MYERS, JOHN LLEWELLYN, 1115 Grand Avenue, Kansas City, Missouri.

1941. (1903) PACKARD, FRANCIS R., 302 South Nineteenth Street, Philadelphia, Pennsylvania.

1940. (1923) SEWALL, EDWARD C., 430 El Escarpado, Stanford University, California.

1948. (1923) SPENCER, FRANK R., Physicians Building, Boulder, Colorado.

1946. (1905) WOOD, GEORGE B., 329 Hathaway Lane, Wynnewood, Pennsylvania.

BENEFACTORS

Dr. Arthur W. deRoaldes

Dr. William E. Casselberry

Dr. Samuel Johnston

Dr. Cornelius G. Coakley

Dr. James E. Newcomb

Dr. John F. Barnhill

Dr. Lee Wallace Dean

Dr. George E. Hourn

BENEFACTORS OF THE MEMORIAL FUND

Dr. John F. Barnhill

Dr. and Mrs. Lee Wallace Dean

Dr. Gordon Berry

Dr. Frederick T. Hill

Dr. and Mrs. George E. Hourn

Dr. Samuel Salinger

Dr. H. Marshall Taylor

Dr. Louis H. Clerf

Obverse of the deRoaldes medal

RECIPIENTS OF THE DEROALDES AWARD

1928. Dr. Chevalier Jackson

1931. Dr. D. Bryson Delavan

1934. Dr. Harris P. Mosher

1937. Dr. Lee Wallace Dean

1943. Dr. Ralph A. Fenton

1949. Dr. George M. Coates

RECIPIENTS OF THE CASSELBERRY AWARD

1923. Dr. George Fetterolf and Dr. Herbert Fox

1928. Dr. Ralph A. Fenton and Dr. O. Larsell

1929. Dr. Richard A. Kern and Dr. Harry P. Schenck

1929. Dr. Edward H. Campbell

1931. Dr. Arthur W. Proetz

1934. Dr. Anderson C. Hilding

1936. Dr. Francis E. Le Jeune: Dr. Joel J. Pressman

1939. Dr. H. Marshall Taylor: Dr. Brien T. King

1940. Dr. French K. Hansel

1941. Dr. Noah D. Fabricant

1946. Dr. Paul H. Holinger

1949. Dr. Henry B. Orton

RECIPIENTS OF THE NEWCOMB AWARD

1941. Dr. Burt R. Shurly

1942. Dr. Francis R. Packard

1943. Dr. George M. Coates

1944. Dr. Charles J. Imperatori

1947. Dr. Harris P. Mosher

1948. Dr. Gordon Berry

1949. Dr. Gordon B. New

PAST OFFICERS

Pesidents

(Year of Electon)

1879. Louis Elsberg
1880. J. Solis-Cohen
1881. F. I. Knight
1882. G. M. Lefferts
1883. F. H. Bosworth
1884. E. L. Shurly
1885. Harrison Allen
1886. E. Fletcher Ingals
1887. R. P. Lincoln
1888. E. C. Morgan
1889. J. N. Mackenzie
1890. W. C. Glasgow
1891. S. W. Langmaid
1892. M. J. Asch
1893. D. Bryson Delavan
1894. J. O. Roe
1895. W. H. Daly
1896. C. H. Knight
1897. T. R. French
1898. W. E. Casselberry
1899. Samuel Johnston
1900. H. L. Swain
1901. J. W. Farlow
1902. J. H. Bryan
1903. J. H. Hartman
1904. C. C. Rice
1905. J. W. Gleitsman
1906. A. W. deRoaldes
1907. H. S. Birkett
1908. A. Coolidge, Jr.
1909. J. E. Logan
1910. D. Braden Kyle
1911. James E. Newcomb
1912. George A. Leland
1913. Thomas Hubbard
1914. Alexander W. MacCoy
1915. G. Hudson Makuen
1916. Joseph L. Goodale
1917. Thomas H. Halsted
1918. Cornelius G. Coakley
1919. Norval H. Pierce
1920. Harris P. Mosher
1921. Harmon Smith
1922. Emil Mayer
1923. J. Payson Clark
1924. Lee Wallace Dean
1925. Greenfield Sluder
1926. Chevalier Jackson
1927. D. Bryson Delavan
1928. Charles W. Richardson
1929. Lewis A. Coffin
1930. Francis R. Packard
1931. George E. Shambaugh
1932. George Fetterolf
1933. George M. Coates
1934. Dunbar Roy
1935. Burt R. Shurly
1936. William B. Chamberlin
1937. John F. Barnhill
1938. George B. Wood

1939. James A. Babbitt
1940. Gordon Berry
1941. Thomas E. Carmody
1942-3. Charles J. Imperatori
1944-5. Harold I. Lillie
1946. Frank R. Spencer
1947. Arthur W. Proetz
1948. Frederick T. Hill

Vice-Presidents

1879. F. H. Davis	
1880. W. C. Glasgow	J. O. Roe
1881. E. L. Shurly	W. Porter
1882. C. Seiler	E. F. Ingals
1883. S. W. Langmaid	S. Johnston
1884. J. H. Hartman	W. H. Daly
1885. H. A. Johnson	G. W. Major
1886. E. C. Morgan	J. N. Mackenzie
1887. J. N. Mackenzie	S. W. Langmaid
1888. W. C. Glasgow	C. E. DeM. Sajous
1889. E. Holden	C. E. Bean
1890. J. O. Roe	J. H. Hartman
1891. M. J. Asch	S. Johnston
1892. S. Johnston	J. C. Mulhall
1893. J. C. Mulhall	W. E. Casselberry
1894. C. C. Rice	S. H. Chapman
1895. J. Wright	A. W. de Roaldes
1896. T. M. Murray	D. N. Rankin
1897. A. W. MacCoy	H. S. Birkett
1898. J. W. Farlow	F. W. Hinkel
1899. T. A. DeBlois	M. R. Brown
1900. H. L. Wagner	A. A. Bliss
1901. J. W. Gleitsmann	D. Braden Kyle
1902. G. A. Leland	T. Melville Hardie
1903. J. H. Lowman	W. Peyre Porcher
1904. Thomas Hubbard	W. J. Freeman
1905. J. L. Goodale	C. W. Richardson

1906. G. H. Makuen
1907. J. P. Clark
1908. E. Mayer
1909. C. G. Coakley
1910. Robert C. Myles
1911. F. C. Cobb
1912. A. W. Watson
1913. F. E. Hopkins
1914. Clement F. Theisen
1915. J. Gordon Wilson
1916. Thomas H. Halsted
1917. John Edwin Rhodes
1918. G. E. Shambaugh
1919. Francis R. Packard
1920. Harmon Smith
1921. Dunbar Roy
1922. George Fetterolf
1923. Hubert Arrowsmith
1924. Ross H. Skillern
1925. John E. Mackenty
1926. Lewis A. Coffin
1927. Charles W. Richardson
1928. Robert Clyde Lynch
1929. William B. Chamberlin
1930. Harris P. Mosher
1931. Joseph B. Greene
1932. Gordon Berry
1933. E. Ross Faulkner
1934. Gordon B. New
1935. Edward C. Sewall
1936. William P. Wherry
1937. Frank R. Spencer
1938. Ralph A. Fenton
1939. John H. Foster
1940. Charles H. Porter
A. B. Thrasher
J. E. Rhodes
F. R. Packard
H. P. Mosher
J. M. Ingersoll
B. R. Shurly
W. Scott Renner
Geo. F. Shambaugh
Lewis A. Coffin
Christian R. Holmes
Greenfield Sluder
D. Crosby Greene
John R. Winslow
Harmon Smith
W. B. Chamberlin
Robert C. Lynch
Lorenzo B. Lockard
Joseph B. Greene
Gordon Berry
Robert Levy
William V. Mullin
Hill Hastings
Francis P. Emerson
Ralph Albert Fenton
James A. Babbitt
E. Ross Faulkner
Frank A. Spencer
Thomas S. Carmody
Samuel McCullagh
H. Marshall Taylor
Harold I. Lillie
Bernard J. McMahon
Frederick T. Hill
Thomas R. Gittins
Gordon F. Harkness

1941. Arthur W. Proetz
1942-3. Harold I. Lillie
1944-5. John J. Shea
1946. H. Marshall Taylor
1947. John J. Shea
1948. Henry B. Orton
Henry B. Orton
Dean M. Lierle
Thomas C. Galloway
C. Stewart Nash
Frederick A. Figi
Anderson C. Hilding

Secretaries and Treasurers

1879. G. M. Lefferts
1882. D. Bryson Delavan
1889. C. H. Knight
1895. H. L. Swain
1900. J. E. Newcomb
1911. Harmon Smith

Secretaries

1912. Harmon Smith
1918. D. Bryson Delavan
1919. J. M. Ingersoll
1920. George M. Coates
1933. William V. Mullin
1935. James A. Babbitt
1939. Charles J. Imperatori
1942. Arthur W. Proetz
1947. Louis H. Clerf

Treasurers

1912. J. Payson Clark
1923. George Fetterolf
1932. William V. Mullin
1933. James A. Babbitt
1935. Charles J. Imperatori
1939. Frederick T. Hill
1948. Gordon F. Harkness

Librarians

1879. F. H. Bosworth
1883. T. R. French
1903. J. H. Bryan
1930. John F. Barnhill
1934. Burt R. Shurly
1935. George M. Coates

Librarian and Historian

1936. George M. Coates
1944. Louis H. Clerk
1947. Harry P. Schenck

PAST MEMBERS

Dates indicate original election to the Association

**Deceased*

Honorary Fellows

*1908. Barnhill, John F., Miami Beach, Florida.
*1893. Birkett, Herbert S., Montreal, Canada.
*1878. Bosworth, Francke H., New York City.
*1918. Dean, Lee Wallace, St. Louis, Mo.
*1881. Delavan, D. Bryson, New York City.
*1893. deRoaldes, Arthur W., New Orleans, La.
*1890. De La Sota Y Lastra, Ramon, Seville, Spain.
*1879. French, Thomas R., Brooklyn, N. Y.
*1880. Garcia, Senior Manuel, London, England.
*1903. Harris, Thos. J., New York City.
*1878. Johnston, Samuel, Baltimore, Md.
*1878. Lefferts, George Morewood, Katonah, N. Y.
*1914. Levy, Robert, Denver, Colo.
*1883. Mackenzie, John N., Baltimore, Md.
*1881. Mackenzie, Sir Morell, London, England.
*1910. Masser, Ferdinand, Naples, Italy.
*1910. Moure, J. J. E., Bordeaux, France.
*1918. Oliver, H. K., Boston, Mass.
*1906. Pierce, Norval Harvey, San Diego, Calif.
*1909. Semon, Sir Felix, Great Missenden, England.
*1878. Solis-Cohen, J., Philadelphia, Pa.
*1889. Swain, Henry L., New Haven, Conn.
*1914. Thomson, Sir St. Clair, London, Eng.
*1903. Tilley, Herbert, London, England.
*1914. Wagner, Clinton, New York City.
*1890. Wright, Jonathan, Pleasantville, N. Y.

Corresponding Fellows

*1892. Browne, Lennox, London, England.
*1940. Colledge, Lionel, London, England.
*1901. Collier, Mayo, Kearsney Abbey, Kent, England.
*1893. Desvernine, Carlos M., Havana, Cuba.
*1930. Emerson, Francis P., Franklin, Mass.
*1936. Fraser, John S., Edinburgh, Scotland.

*1901. Grant, Sir James Dundas, London, England.
*1887. Cougenheim, A., Paris, France.
*1894. Holden, Edgar, Newark, N. J.
*1919. Kelly, Adam Brown, Helensburgh, Scotland.
*1881. Labus, Carlo, Milan, Italy.
*1931. LasSagna, Francesco, Parma, Italy.
*1926. Law, Frederick M., New York, N. Y.
*1902. Lermoyez, Marcel, Paris, France.
*1897. Luc, H., Paris, France.
*1896. MacDonald, Greville, Haslemere, Surrey, England.
*1894. MacIntyre, John, Glasgow, Scotland.
*1903. McBride, P., York, England.
*1920. McKenzie, Dan, London, England.
*1919. McKernon, James F., New Canaan, Conn.
*1880. Meyer, Wilhelm, Copenhagen, Denmark.
*1896. Mygind, Holger, Copenhagen, Denmark.
*1919. Paterson, Donald Rose, Cardiff, Wales.
*1919. Rogers, John, Jr., New York City.
*1894. Sajous, C. E. DeM., Philadelphia, Pa.
*1896. Schmiegelow, Ernst, Copenhagen, Denmark.
*1946. Segura, Eliseo, Buenos Aires, Argentina.
*1940. Soto, E. Fernandez, Havana, Cuba.
*1881. Thornton, Pugin, London, England.
*1913. Turner, A. Logan, Edinburgh, Scotland.
*1880. Whistler, W. McNeil, London, England.
*1901. Wingrave, Wyatt, Lyme Regis, Dorset, England.
*1894. Wolfenden, R. Norris, Kent, England.

Emeritus Fellows

*1928. Beck, Joseph C., Chicago, Illinois.
*1901. Brown, J. Price, Toronto, Canada.
*1891. Bryan, Joseph H., Washington, D. C.
*1897. Clark, J. Payson, Boston, Mass.
*1899. Cobb, Frederick C., Bradenton, Florida.
*1905. Coffin, Lewis A., New York City.
*1893. Coolidge, Algernon, Boston, Mass.
*1913. Dabney, Virginius, Washington, D. C.
*1882. De Blois, Thomas Amory, Boston, Mass.
*1892. Farlow, John W., Boston, Mass.
*1922. Forbes, Henry H., New York City.

*1905. Freer, Otto T., Chicago, Ill.
*1880. Gleitsmann, Joseph W., New York City.
*1906. Greene, D. Crosby, Jr., Boston, Mass.
*1896. Hardie, Thomas Melville, Chicago, Ill.
*1915. Hastings, Hill, Los Angeles, Calif.
*1888. Hinkel, Frank Whitehill, Buffalo, New York.
*1895. Hopkins, Frederick E., Springfield, Mass.
*1927. Hubbard, Thomas, Toledo, Ohio.
*1919. Hurd, Lee Maidment, Rowayton, Conn.
*1904. Ingersoll, John Marvin, Miami, Fla.
*1918. Kenyon, Elmer L., Chicago, Ill.
*1929. Kistner, Frank B., Portland, Oregon.
*1885. Knight, Charles H., New York City.
*1939. Large, Secord H., Cleveland, Ohio.
*1894. Leland, George A., Boston, Mass.
*1943. Lincoln, William R., Cleveland, Ohio.
*1886. MacCoy, Alexander W., Philadelphia, Pa.
*1896. Mayer, Emil, New York City.
*1943. McCullagh, Samuel, New York, N. Y.
*1923. McKinney, Richmond, Memphis, Tenn.
*1878. Porter, William, Ocean Springs, Miss.
*1901. Myles, Robert C., New York City.
*1923. Newhart, Horace, Minneapolis, Minn.
*1942. Potts, John B., Omaha, Nebr.
*1903. Renner, W. Scott, Buffalo, N. Y.
*1897. Rhodes, John Edwin, Chicago, Ill.
*1884. Rice, Clarence C., New York City.
*1905. Richards, George L., South Yarmouth, Mass.
*1878. Robinson, Beverly, New York City.
*1907. Shambaugh, George E., Chicago, Ill.
*1908. Smith, Harmon, New York City.
*1892. Wagner, Henry L., San Francisco, Calif.
*1892. Watson, Arthur W., Philadelphia, Pa.
*1939. Wilson, J. Gordon, Old Bennington, Vt.

Active Fellows

*1880. Allen, Harrison, Philadelphia, Pa.
*1917. Arrowsmith, Hubert, Brooklyn, N. Y.
*1879. Asch, Morris J., New York City.
*1923. Babbitt, James A., Philadelphia, Pa.

*1906. Ballenger, William L., Chicago, Ill.
*1880. Bean, C. E., St. Paul, Minn.
*1904. Berens, T. Passmore, New York City.
*1924. Bigelow, Nolton, Providence, R. I.
*1893. Bliss, Arthur Ames, Philadelphia, Pa.
*1895. Boylan, J. E., Cincinnati, Ohio.
*1892. Brown, Moreau R., Chicago, Ill.
*1933. Buckley, Robert E., New York City.
*1915. Canfield, R. Bishop, Ann Arbor, Mich.
*1934. Carmack, John Walter, Indianapolis, Ind.
*1924. Carmody, Thomas E., Denver, Colo.
*1889. Casselberry, William E., Chicago, Ill.
*1883. Chamberlain, C. W., Hartford, Conn.
*1917. Chamberlin, William B., Cleveland, Ohio.
*1896. Chappell, W. F., New York City.
*1882. Chapman, S. Hartwell, New Haven, Conn.
*1902. Coakley, Cornelius G., New York City.
*1913. Coffin, Rockwell C., Boston, Mass.
1918. Cox, Gerald H., New York City.
*1880. Cushing, E. W., Boston, Mass.
*1878. Cutter, Ephraim, West Falmouth, Mass.
*1880. Daly, W. H., Pittsburgh, Pa.
*1878. Davis, F. H., Chicago, Ill.
*1941. Davis, Warren B., Philadelphia, Pa.
1926. Dennis, Frank Lownes, Colorado Springs, Col.
*1901. Dickerman, E. T., Chicago, Ill.
*1878. Donaldson, Frank, Baltimore, Md.
*1935. Eves, Curtis C., Philadelphia, Pa.
*1919. Faulkner, E. Ross, New York City.
*1914. Fetterolf, George, Philadelphia, Pa.
*1901. Freeman, Walter J., Philadelphia, Pa.
*1917. Friedberg, Stanton A., Chicago, Ill.
1940. Fuchs, Valentine H., New Orleans, La.
1909. Getchell, Albert C., Worcester, Mass.
*1897. Frothingham, Richard, New York City.
*1907. Gibb, Joseph S., Philadelphia, Pa.
*1878. Glasgow, William Carr, St. Louis, Mo.
*1913. Goldstein, Max A., St. Louis, Mo.
*1905. Grayson, Charles P., Philadelphia, Pa.
*1878. Hartman, Jacob H., Baltimore, Md.

*1879. Holden, Edgar, Newark, N. J.
*1907. Holmes, Christian R., Cincinnati, Ohio.
*1882. Hooper, Franklin H., Boston, Mass.
*1893. Hope, George B., New York City.
*1938. Hourn, George E., St. Louis, Mo.
*1901. Hyatt, Frank, Washington, D. C.
*1925. Iglauer, Samuel, Cincinnati, Ohio.
*1878. Ingals, E. Fletcher, Chicago, Ill.
*1882. Ives, Frank L., New York City.
*1880. Jarvis, William C., New York City.
*1878. Johnson, Hosmer A., Chicago, Ill.
*1879. Johnson, Woolsey, New York City.
*1879. Kealhofer, R. H., St. Louis, Mo.
*1901. King, Gordon, New Orleans, La.
*1885. Knight, Charles H., New York City.
*1878. Knight, Frederick Irving, Boston, Mass.
*1898. Kyle, D. Braden, Philadelphia, Pa.
*1880. Langmaid, Samuel W., Boston, Mass.
*1878. Lincoln, Rufus P., New York City.
*1911. Lockard, Lorenzo B., Denver, Colo.
*1913. Loeb, Hanau W., St. Louis, Mo.
*1897. Logan, James E., Kansas City, Mo.
*1888. Lowman, John H., Cleveland, Ohio.
*1919. Lynah, Henry L., New York City.
*1915. Lynch, Robert Clyde, New Orleans, La.
*1879. McBurney, Charles, New York City.
*1927. McGinnis, Edwin, Chicago, Ill.
1936. McGregor, Gregor, Toronto, Canada.
*1913. McKimmie, O. A., Washington, D. C.
*1885. McSherry, H. Clinton, Baltimore, Md.
*1914. Mackenty, John E., New York City.
*1898. Makuen, G. Hudson, Philadelphia, Pa.
*1881. Major, G. W., Montreal, Canada.
*1881. Morgan, E. C., Washington, D. C.
*1886. Mulhall, J. C., St. Louis, Mo.
*1925. Mullin, William V., Cleveland, Ohio.
*1914. Munger, Carl E., Waterbury, Conn.
*1892. Murray, T. Morris, Washington, D. C.
*1881. Mynter, H., Buffalo, N. Y.
*1893. Newcomb, James E., New York City.

*1895. Nichols, J. E. H., New York City.
*1894. Park, William H., New York City.
*1892. Porcher, W. Peyre, Charleston, S. C.
*1927. Porter, Charles T., Boston, Mass.
*1908. Randall, B. Alexander, Philadelphia, Pa.
*1882. Rankin, D. N., Allegheny, Pa.
*1902. Richardson, Charles W., Washington, D. C.
*1879. Roe, John O., Rochester, N. Y.
*1881. Robertson, J. M., Detroit, Mich.
*1913. Roy, Dunbar, Atlanta, Ga.
*1878. Rumbold, T. F., St. Louis, Mo.
*1879. Seiler, Carl, Philadelphia, Pa.
*1893. Shields, Charles M., Richmond, Va.
*1878. Shurly, E. L., Detroit, Mich.
*1892. Simpson, William Kelly, New York City.
*1919. Skillern, Ross H., Philadelphia, Pa.
*1909. Sluder, Greenfield, St. Louis, Mo.
*1879. Smith, Andrew H., Geneva, N. Y.
*1932. Smyth, Duncan Campbell, Boston, Mass.
*1928. Sonnenschein, Robert, Chicago, Ill.
1924. Stein, Otto J., Chicago, Ill.
1934. Stevenson, Walter, Quincy, Ill.
*1911. Staut, George C., Philadelphia, Pa.
*1879. Tauber, Bernhard, Cincinnati, Ohio.
*1903. Theisen, Clement F., Albany, N. Y.
*1899. Thorner, Max, Cincinnati, Ohio.
*1892. Thrasher, Allen B., Cincinnati, Ohio.
*1937. Tobey, George L., Jr., Boston, Mass.
*1888. Van der Poel, S. O., New York City.
*1938. Vail, Harris H., Cincinnati, Ohio.
*1936. Voislawsky, Antonie P., New York City.
*1933. Wanamaker, Allison T., Seattle, Wash.
1896. Ward, Marshall R., Pittsburgh, Pa.
*1879. Ward, Whitfield, New York City.
*1886. Westbrook, Benjamin F., Brooklyn, N. Y.
*1924. Wherry, William P., Omaha, Neb.
*1924. White, Leon E., Boston, Mass.
*1922. Wishart, David J. G., Toronto, Ontario.
*1940. Wood, V. Visscher, St. Louis, Mo.
*1896. Wollen, Green V., Indianapolis, Ind.

G.F.TUCKER