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## Etiology of otosclerosis

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THE  
ETIOLOGY  
OF  
OTOSCLEROSIS

L.H.Heine.

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## INTRODUCTION

In writing this summary of the literature on the etiology of otosclerosis it was the hope that a general knowledge of the theories advanced up to the present might be obtained. That by this means the progress in this field might be evaluated and that some of the problems presenting themselves in the treatment of otosclerotic patients made easier.

Otosclerosis always has been a social problem and sooner or later every physician is confronted with the responsibility of advising some patient suffering from the disease.

Is the disease inherited? Is treatment therefore of no avail and must we look forward to unfavorable prognosis in all cases? Should a patient with otosclerosis marry and have children? Would pregnancy incite otosclerosis in the mother? Or if she has otosclerosis would it contribute to the advancement of the disease?

To what extent are we able to prevent otosclerosis by eliminating possible etiological factors?

Moreover, otosclerosis is characterized by certain psychic changes, notable mental depression and an attempt to limit all social intercourse. Are these changes the result of the condition of being deaf, or are the changes just as much the part of otosclerosis as the changes in the labyrinthine capsule? Questions like the above can only be answered by studying the etiology of the condition.

The work presented here begins with the earliest work done on the subject and as nearly as possible each reference is added more in its place in the development of the literature than the real subject matter it contains.

The work of the "Committee on Otosclerosis" of the American Otological Society has been used constantly for material. The manner of presenting the subject under Heredity causes, Congenital causes, Local causes, and General causes was suggested by this same work.

## HEREDITARY CAUSES

In 1860 Toynbee reported two cases of stapes ankylosis, in which there was a history of deafness in the family.

Keene in 1873 made the statement that is is an "undoubted fact" that the condition is hereditary.

Von Troeltsch at about the same time said that chronic aural catarrh is hereditary and results in the condition known as otosclerosis.

Hammerschlag beginning in 1906 reported many genealogies all bearing out his contention that the affection appears more or less frequently in certain families through several generations. He maintained that otosclerosis and hereditary deafmutism are different manifestations of the same process.

1. Degenerative-atrophic processes in nerve and nerve terminals found in deafmutism are entirely the same as those found in otosclerosis.
2. The characteristic bone changes of otosclerosis in the labyrinthine capsule are also found in some cases of congenital deafness.
3. There are families in which hereditary deafness and otosclerosis are associated.

If Siebenmann's interpretation of otosclerosis be correct, in that it is an abnormal post embryonic process of growth, then we have a condition definitely favoring the theory of its hereditary transmissibility. Any process of growth, normal or abnormal, must be provided by a determinant in the germ plasm of the individual and must therefore be transmissible by heredity. The essential efficiency of this determinant and the time of its manifestation are presumably of internal or external kind. Thus, pregnancy or puberty may become an exciting factor. Perhaps social diseases may precipitate the abnormal process of growth in certain cases.

The law of heredity is applicable even to those cases of otosclerosis in which no heredity is demonstrated; the apparently spontaneous cases of otosclerosis are explained simply by latent inheritance.

We must not lose sight of the fact that the germ plasm of every human being is very complex in the number of determinants; so that the germ plasm of every human must contain the otosclerosis determinant, which may once again become operative after generations.

However, the law of heredity explains the nature of otosclerosis only in so far as it indicates the transmissible abnormal process of growth.

Katz stated he is convinced that the bony changes in otosclerosis are based upon a constitutional usually hereditary disease, on the basis of which the temporal bone or auditory organ enclosed in it represents a point of diminished resistance acted upon by a series of injurious factors.

Alexander and Lindt in 1906 reported some cases of deafmutism in which otosclerotic foci were found in the labyrinthine capsule. Alexander claimed that the findings are important in the interpretation of otosclerosis and maintained that otosclerosis is a hereditary affection which does not develop clinical signs until puberty. Believing that the otosclerotic patient even as a child, as a fetus, shows strongly vascularized bone foci in his petrous bone and that at the time of puberty these advance to the labyrinthine endostium leading to fixation of the stapes, changes in the oval window and the secondary nerve changes.

The evidence is not in favor of otosclerosis as being a dominant factor nor is it a sex linked factor, nor a pure recessive factor, but rather the constitutional basis represents two recessive factors.

A review of the evolution of the organ in vertebrates shows that the semicircular canals and vestibule have reached their full development in the fish. The oval and round windows and ossicles have all been evolved since the amphibians.

Coray said that otosclerosis is a biological variation, and stated that variations are apt to occur in recent biological origin.

This would explain the fact that otosclerosis involves the foot plate of the stapes, the bony wall of the cochlea, while the other portions of the labyrinth are almost untouched. Thus we may have an explanation of the fact that the condition may arise spontaneously and yet be transmitted. Further consideration of the theory shows the "primary fault" in otosclerosis is an inherent defect in the living cells of the organ of hearing.



Anemia, pregnancy, syphilis, toxins, exposure, abnormal internal secretions, and middle ear conditions are necessary for its occurrence. However, they may make manifest the tendency that may otherwise remain latent.

Gray in a review of the various theories of the etiology of deafness, concluded that " otosclerosis is a definite pathological change in the bony capsule of the labyrinth, bilaterally symmetrical making its appearance very gradually and occurring in individuals who may be in ill health from widely different causes, but often in those who are in the best of health." The majority of individuals do not develop otosclerosis no matter the condition of health or the occurrence of local disease in the ear.

Logically the basic cause of the disease must be found in the organ of hearing itself, and this cause must be in certain individuals only. The constant factor being the inborn tendency. Many conditions may precipitate the disease, but there is no other constant factor.

Albrecht names two possibilities.

1. Only the disposition to hardness of hearing is hereditarily transmitted, and that its development depends upon the acquired damage.
2. If the capacity for development is inherited it might be assumed that the germ plasm of otosclerosis in a very general way possesses the ability to produce transformation of the bone in the labyrinthine capsule, but that this transformation does not necessarily develop in localities which lead to the development of hardness of hearing.

Therefore, in sporadic cases of otosclerosis bone foci had also developed in the parents, grandparents, sisters, brothers, but did not become manifest.

The author however does not believe it is very plausible that bone foci in one family develop in areas of any importance.

Concluding that the assumption of a uniform hereditary transmission will have to be abandoned, it is probable that besides the dominant type, a recessive type of transmission does occur.

Constitutional sporadic deafmutism shows a monohybrid recessive heredity. In hereditary labyrinthine hardness of hearing, a dominant heredity can be recognized.

From Gradenigo's study we learn that the transmission of otosclerosis is apparently due to a single factor, and is transmitted as a recessive character. In this type the disease is latent in some members of the family, who may however transmit it.

The disease becomes manifest on the union of two apparently healthy transmitters, or on the union of a transmitter and a patient in the affected offspring. While a transmitter and a healthy individual produce only transmitters, the number of transmitters has no tendency to diminish in successive generations. That there is a great divergence of opinion as to the mode of transmission of otosclerosis there can be no doubt. Many authors followed genealogies presenting pure evidence of the trait being present as a dominant one, while others presented just as great an argument for the trait being recessive.

The latest work in 1928 by Haike, rather supports the view that the trait is apparently, monohybrid, and recessive in many cases.

Perhaps the chaotic state may be explained by the fact that different hereditary dispositions to otosclerosis have different geographical or ethnic distribution. Further investigations over larger material after further conquering the many troublesome factors influencing human heredity must be undertaken and may furnish a simpler possibility of interpretation, of the apparently complicated problem.

Haike referred to the work of Hammerschlag and Koemer, from which we have learned that otosclerosis appears on a foundation of poor constitution and is often accompanied by other hereditary anomalies and constitutional diseases. Haike's studies are not much more than support to the foregoing. He likewise noted that a peculiarity of otosclerotic families was longevity. Likewise he also noted a great fecundity in these families not so much so with the otosclerotics themselves but with their relatives. He concluded that otosclerosis is a recessive and not a dominant characteristic.

Undritz contributed an article in which he stressed the frequency of occurrence of other degenerative conditions in various organs in other members of the same families.

Harris is of the opinion that far too much has been accepted by tradition or upon the authority of others in the matter of heredity in otosclerosis.

In 1929 at which time he had concluded two years of careful study of familial histories of every case presenting itself he stated that of the cases referred for study representing all or most of the cases of progressive deafness presenting themselves during three days of the week at one of New York's largest hospitals the number of those with clear history of familial deafness is far below fifty.

Far too many cases are accepted as being familial when closer examination would show that deafness in the grandparents and other relatives resulted from injuries or other diseases.

Thereby accounting for the prevailing opinion that inheritance is a constant factor, naturally such a belief improves the prognosis of those suffering from the disease.

However, when a history is obtained, the prognosis for recovery is difficult and progress of the deafness is apt to be enhanced.

## CONGENITAL CONDITIONS IN LABRINTHINE CAPSULE

As early as 1872 Wendt noted that the anatomical condition of the niches of the windows of the labyrinth as well as the distance between the tegmen and head malleus and body of the incus and the dimensions of the tympanic cavity in general facilitated the occurrence of abnormal adhesions.

Especially in favor of the origin of adhesions of stapes to the adjacent bony wall, is an unusual depth of the niche of the oval window.

Gradenigo has found that the stapes is derived from fusion of two distinct morphological elements, the stapedia ring being derived from the second branchial arch, and the stapedia lamina or foot plate from the labyrinthine capsule. The chief lesions of sclerotic otitis involve the vestibular wall of the tympanic cavity and the stapes, namely parts which show a complex embryonic development, the usual site of the lesion therefore is determined morphologically. Likewise the same author states that the bands and membranes in cases of otosclerosis must not be regarded as newly formed, but simply as a residue of the embryonic gelatinous tissue. This is found by special study of the arrangement of the gelatinous tissue of the temporal bones in human and mammalian embryos, in new-born infants and in adults.

The author concludes, that in human embryos of a length of 4-4 $\frac{1}{2}$  cm., when the process of chondrification of the primitive skeleton of the ear has barely begun, there is a true tympanic cavity, in the form of a narrow slit, along the tympanic membrane, approximately at the level of the lower portion of the promontory and the fossae of the round window. This slit is lined with epithelium and represents the posterior extremity of the tubo tympanic canal. It is prolonged backwards as far as the frontal plane of the stapes and the posterior border of the tympanic ring.

At this time, the mesoblastic tissue which fills the internal ear begins to become absorbed in the vestibule at the level of the future perilymphatic cistern of the labyrinthine aspect of the membrane of the round window. In embryos of 7 $\frac{1}{2}$ -8 cm., the mesoblastic tissue of the labyrinth is completely absorbed around the constituents of the vestibule and the gyrus basilaris cochlearis, persisting in part along the upper turns of the cochlear canal and the membranous semicircular canals.

Up to birth the ossicles are still surrounded by mesoblastic tissue which fills the fossae of the two windows and covers the promontory. In man a rapid absorption of this tissue does not take place until after birth, and then is not always complete.

On examination of the tympanic cavities of new born infants it can be seen that in some cases this absorption has been complete and that the ossicles, and fossae of the two windows appear clear. While in others strands of gelatinous tissue remain in various configurations. All these bands and membranes show exactly the same arrangement as the embryo. These remnants may undergo atrophic changes in extra uterine life, but several of the residues may be encountered in adults.

The adhesions in the author's cases of otitic sclerosis presented features so much like those in the embryonic stages, that they should be considered not as new formations but as remnants of fetal tissue.

Bruhl and Gebhardt interpreted stapes ankylosis as the effect of traction and pressure. The region of the stapes foot plate was found to favor a high degree the formative stimulus for transformation and formation of bone. The anatomy whereby the cartilage covered stapes plate is fixed by tendinous connective tissue bundles at the vestibular window while the tensor tympani muscle lies at the anterior circumference of the stapes, the tendon which passes across the cochlearform process to the malleus. Moreover, the annular ligament is broader anteriorly than posteriorly so that the movement is more pronounced in front than behind. The anterior vibration of the base of the stapes in hearing and the contraction of the tensor tympani muscle, gives rise to persistent irritation of periostium on the bone between the tendon of the muscle and annular ligament of the stapes. Therefore we have an often repeated formative stimuli.

The view is well supported by the fact that otosclerosis is exceptional in persons who, because of loss of tympanic membrane and inactivity of tensor tympani muscle, have no chronic formative or stimulation of action on the bone. The reason why such changes do not occur in all cases is do to hereditary disposition. Asuming then a hereditary factor, various factors can probably act as a stimulus to new bone formation.

Many writers, the most prolific perhaps being Manasse, reported cartilage rests in the labyrinthine capsule.

These rests can definitely be traced back as far as a three months embryo. Closely related to these foci are usually found small bone foci immature bone, nonosteoid and containing fat marrow spaces. The peculiar bone he interprets as pathologically incomplete ossification, the foci as embryonic arrests.

The site of such foci certainly suggests an etiological relationship to otosclerosis, the more so as heredity is considered a factor in the disease. Certainly the conclusion that these cartilage remnants represent the arrested development of variable etiology and are a point of diminished resistance to the otosclerotic process or even a preliminary stage of this process seems justified.

Such an explanation affords support in the uniformity of the location of the disease, its hereditary character and its association with other conditions as cleft lip and etc.

Mayer in a series of articles, in which he thoroughly studies the embryological development of the labyrinthine capsule, strongly supports his theory that the otosclerotic foci are to be interpreted as proliferations that develop from embryonic tissue malformations and designate them as hamartomas. The otosclerotic foci originate through proliferation of an embryonic malformed osteoplastic tissue found as a rule in definite localities of the labyrinthine capsule.

Through this proliferation the old bone is absorbed on the one hand while on the other, new bone is formed again, the process keeping to the limits of the old bone, so that a transformation occurs along a pathological course.

Some other factors favor this interpretation:

1. Other hyperplastic bone proliferations may be encountered in the petrous bone, that is exostoses, at the posterior pyramidal



surface, in the internal auditory meatus or in the tympanic cavity.

2. Malformations of the cochlear spindle along with deafmutism.

All the above have been reported simultaneously with the finding of otosclerotic foci. Mayer then says that this malformation represents a positive sign of a change originating in the course of embryonic development, therefore the conclusion is justified that otosclerotic foci represents malformation or proliferations derived from such.

The otosclerotic foci form a concomitant phenomenon of severe developmental disturbances of the ear, on the one hand, while on the other hand more or less marked malformations of the ear are found in otosclerosis.

Attention is called to the fact that such conditions as multiple exostoses are hereditary. These lesions are interpreted as a degenerative sign and are found in individuals who present other degenerative stigmata. The cause of atrophy of the labyrinth and internal ear usually found in otosclerosis is also referable to a faulty anlage which manifests itself in certain malformations and also in a very peculiar tendency of connective tissue ossification.

Therefore otosclerosis may also be grouped under the heading of hereditary degenerative processes.

The degeneration affecting the entire organ and manifesting itself by the labyrinthine capsule becoming abnormally transformed on the basis of embryonic tissue malformation.

On this basis Mayer concludes "Not only the histological character of the foci, but also the multiplicity, the typical

localization and symmetry the existence of minute islands of atypical tissue at the sites of origin of the foci, furthermore also the simultaneous occurrence of malformations in the internal ear and in other regions of the auditory organ, as well as the hyperplasia of the entire petrous bone, the clinically established association with congenital signs of degeneration and finally heredity are in favor of the assumption that the foci are to be interpreted as tumor, like hyperplasias." Working with such a theory we place otosclerosis on a basis of general pathology, for the author's theory is linked with known processes in other systems of the organism.

Just why large otosclerotic foci develop from embryonic malformed osteoblastic tissue in some cases while in others the growth advances only partially or stops, we can not say. This question as to growth of the foci is the same problem that confronts us with the growth of tumors and their origin from tissue malformations, it is still a general pathological problem as yet unsolved.

Mayer in a paper on the pathology of otosclerosis gives his interpretation of the condition as follows:

"The original bone of the labyrinth capsule becomes absorbed by osteoclasts and a bone marrow is formed, in which an excessive number of osteoblasts abound. In this marrow the new bone is formed but it is imperfect. It is reticulated, stains dark blue with haemalin and eosin, and contains a number of irregular bone cells. This imperfect new bone gradually becomes surrounded by more perfect bone.

Such tissue as the blue staining bone is never seen in the normal labyrinth capsule or in other pathological conditions. It is this fact which gives us the key to the disease, since it can thus represent neither a physiological transformation nor an inflammatory development.

Physiological transformation and regeneration processes of bone develop in quite a different way. Never, in discreet foci, but always in irregularly dispersed canal systems. In physiological transformations and inflammatory conditions, new blood vessels enter the canals of the old bone. Further in otosclerosis there is no exudation such as occurs in cases of inflammation, and the bone spaces contain not granulation tissue, but an osteoblastic marrow.

Guggenheim in 1931 studied the organ of hearing from the lowest vertebrate to man. From this study he makes the following conclusion:

'That certain chromosomes transmit a something which causes the oval window to close with bone. The typical site is just anterior to the foot plate of the stapes. The new bone is a fibre or web bone. It obliterates the oval window by replacing the foot plate and annular ligament. The labyrinth becomes shut off as far as its primitive portion (vestibular apparatus) is concerned: just as it is shut off in the lower vertebrates.'

"May we not, therefore, look upon otosclerosis as a regression rather than a disease process?"

## INFLUENCE OF LOCAL CONDITIONS

Toynbee in his studies concerning the pathology of otosclerosis, notes as a rule that the mucous membrane of the tympanic cavity is thickened and that the tympanic membrane is often opaque and somewhat thickened.

Thus suggesting some chronic initiating factor: that is, inflammation which if not removed may cause some varieties of stapes ankylosis.

Morphologically there is a close relationship between the tympanic mucosa and the adjacent portion of the petrous bone. Moreover, the vascularization of these parts is closely connected so that any disease of the mucosa or nutritional disturbance would react upon the closely connected periosteum and bone itself.

Middle ear catarrh may be a frequent cause of stapes ankylosis. In this disease the entire mucous covering of the stapes and annular ligament is involved. In severe cases a deposit of calcium salts takes place so that the tympanic membrane and stapes becomes rigid and immovable. Likewise there may be the formation of adhesive bands between the crura of the stapes and especially the niche of the oval window. Many cases of stapes ankylosis have been reported as due to secondary catarrh from the naso pharynx extending up the Eustachian tube.

Steinbrugge is of the opinion that permanent changes in the tympanic mucosa may result from frequent recurrence of catarrhal inflammation, as well as in consequence of chronic hyperemia.

The connective tissue fibers become denser and contain calcium concretions; and deposits form on the labyrinthine walls, often as circumscribed hyperostotic formations.

These sclerotic changes may also develop without preceding inflammatory processes. The tympanic mucosa may not be involved or only to a slight degree. However, there is often congestion of the vessels in the handle of the malleus and a chronic hyperemia of the mucosa of the labyrinthine wall.

Grunert in 1903 and 1904, believed that otosclerosis as a sequel to middle ear disease was unsupported and that the nucleus of the disease consisted of very definitely circumscribed pathological foci extending deeply into the petrous bone and not in immediate contact with middle ear mucosa. In some cases however a preceding otitis media may have been a causative factor in eliciting the characteristic bone disease in the presence of an inherited predisposition.

Nevertheless acute purulent otitis media, usually extends to the cellular spaces, pneumatic and marrow spaces adjoining the middle ear, while the labyrinthine capsule presents slight changes as a result of congestive hyperemia and eventually becomes involved either by way of middle ear or cellular spaces.

Gray stated in 1906, that the circulation in the minute vessels of the bone in the labyrinthine capsule is very apt to become sluggish or to cease altogether, for a time;

thrombosis may occur in the blood vessels or capillaries and the portion of bone supplied by these vessels, would die. Not being infected the dead piece of bone would be surrounded by a line of demarcation and be absorbed, followed by a laying down of new bone.

The circulation in the labyrinthine capsule is particularly prone to stasis, since the walls of vessels in bone cannot collapse and when the force of circulation is not sufficient to force blood through, the latter must stagnate. Because of the narrowness of the Haversian canals in the temporal bone the force required to drive the blood through is much greater due to the great amount of friction to be overcome. The fixation of the stapes in the oval window is easily explained by this hypothesis. Certain local and general conditions favor these pathological changes. Certain individuals or families may have narrower capillaries in the bone than others. There may be differences in the viscosity of blood. It is quite possible that affection of the muco-periostium with cicatricial contraction of the tissue might act on the smaller arteries before they penetrate bone and diminish the force of the blood current.

Bryant's clinical observation and laboratory studies, have led him to conclude, the pathology of this condition depends upon vascular disturbances, confined to one or more of the following regions: the drum membrane, the major ossicles, the stapes and labyrinthine walls. The trophic changes resulting are, congestion, vascular proliferation, infiltration, interstitial inflammation, hyperplasia, contraction, compression of blood vessels, anemia, degeneration, calcification, vascular osteitis or osteoporosis, and hyperostosis.

He concludes that the condition may be hereditary since it depends upon nervous instability and morphological irregularities, qualities which are hereditary to a degree.

The etiology of these mucous membrane disturbances is varied, the chief etiology factor is reduced patency of the Eustachian tube causing circulatory disturbance in the tympanum; next are inflammatory changes in the tympanic mucosa with fibrosis. Less frequent is altered vaso motor action in the middle ear due to impaired function of the general or sympathetic nervous system, from general or nervous exhaustion.

In a later paper the same author classified chronic catarrhal otitis media and otosclerosis in two groups on the basis of etiology and pathology:

(1) catarrhal and (2) trophotoxic. Group I includes cases caused by disturbances of the mucous membrane of the upper air tract, which affects the middle ear either by local inflammation or improper drainage and ventilation through the auditory tube. Group II includes cases caused by trophic and toxic disturbances affecting the mucous membrane and subjacent portions of the middle ear. The etiology factor in group I may be, inflammatory lesions spreading through the auditory tube to the tympanum or obstructive lesions; that is, tonsils, adenoids, and etc. Group II may be general or local in the ear, naso pharynx, in sympathetic nerves or in unbalanced internal secretions. Pathologically they are about the same. One exception being noted in the catarrhal group fibrous hypertrophy of the mucous membrane is more marked: in the tropho-toxic cases, bone changes and atrophy are the most marked.

Mayer, like Bryant strongly supports the view that the condition is one of local vascular disturbance. A local circulatory disturbance

will also account for another fact, that certain sharply outlined portions of the boney capsule of the cochlea remain permanently free from disease. Assuming that the bone of the petrous bone is changed because of poor nourishment, portions having a better blood supply should escape this change. This is probably why spongy bone is never found diseased in otosclerosis, the process always being found in compact bone. Another indication of circulatory disturbance is the presense of hemorrhages in the foci, and the often described hyperemia of definite portions of the diseased bone.

The deficient local blood supply may be due to vaso motor disturbances or organic changes in the blood vessles, which may result from general conditions or from inflammations of the middle ear. A very surprising statement is made by Gradengo, who stated that his clinical studies had led him to the conclusion that tuberculosis was usually present in families of otosclerotic patients, although evidence of the disease is rarely found in the patients themselves. This tuberculosis diathes~~is~~ leads to diminished resistance of the upper air passages as illustrated by the frequency of adenoids. The author distinguishing three types of adenoids with reference to their relation to the ear:

1. Adenoids, which have merely a local action on the lower nasal passages.
2. Adenoids, which nasopharyngeal changes involve the tympanum and middle ear giving rise to dry or purulent inflammations with out extension to the labyrinthine windows.
3. Adenoids, which affect the middle ear so as to extend to the labyrinthine windows and often result in otosclerosis.



This view is supported by the repeated clinical finding of adenoids, in adult patients, with otosclerosis. There are of course cases of otosclerosis which neither histological examination nor clinical findings indicate inflammatory lesions of the mucosa. Catarrhal and inflammatory conditions leading from early childhood may leave no macroscopic or microscopic changes in the labyrinthine capsule. In order to consider a catarrhal affection of the middle ear as an etiological factor, this disturbance need not be of any considerable degree. It is probably that in certain cases, relatively unimportant changes of the tympanic mucosa, vascular or trophic in character favor the development of the otosclerotic bone lesions in predisposed individuals. According to some scientists otosclerosis represents a different disease than chronic otitis media, to others they are the one and same thing. While Gradeningo points out that although otosclerosis is something different from chronic otitis they are closely related, the otitis representing the "preparation and requisite basis for the ultimate development of otosclerosis."

Raoult in 1912 found neuritis of the peripheral nerves and of the eighth pair, and atrophy of the muscles of the ear, in otosclerosis. He is of the opinion that in otosclerosis there is usually a neuritis of the sensory otitic plexus of motor branches and of the terminations of the auditory nerve, especially of the vaso motor fibers.

Whenever one or the other of these nerve elements is affected, function is disturbed, in regard to transmission and accommodation to sounds and auditory receiving apparatus.

Neuritis of sensory and trophic nerves results in anemia of the middle ear and tympanic membrane. There follows then all the trophic changes of otosclerosis. Neuritis of the motor nerves immobilizes the muscles of accommodation resulting in ankylosis of the ossicles

and in the diminuation of the circulation and the resulting trophic changes mentioned above.

Jenkins in 1913 stated that he had found cases with typical symptoms of otosclerosis that disclosed no evidence of fixation of the stapes: also that cases of post suppurative fixation do not show paracusis as a rule. He has concluded that changes in the labyrinthine fluid are responsible for the clinical features of otosclerosis and that changes of the foramen ovale and elsewhere are later and secondary changes.

Suppose this fluid to become of increased specific gravity, then the inertia might be so great as to cause defective hearing of sounds through the middle ear, while the more dense fluid would favor bone conduction. The increased density would likewise, explain the symptom of paracusis. An increased noise would set this denser fluid in increased molecular motion, rendering it more suitable for the transmission of the voice vibrations.

The author has found that if water is run into the external meatus first at body temperature and gradually increasing up to the limit of the patients endurance and continued for five minutes that hearing was immediately improved but only temporarily. The hot water diminishing the density and increasing the molecular movement of the labyrinthine fluid.

Wittmaack in 1919 on the basis of his pathology studies concluded that venous stasis originating in the venous sinus near the labyrinthine capsule produced the pathological changes. For years he endeavored to produce the condition by animal experimentation. First he attempted to injure the trophic nerves, supplying the bone substance, but all these experiments gave negative results.

Much by accident he observed that when he attempted to inject Chinese ink into the semicircular canals of fowls, that he missed the canal and injured the venous blood sinus which passes in a bony channel near the semicircular canal. In these cases microscopic examination showed changes entirely similar to otosclerosis. There followed then a long series of experiments in which various methods were used to produce venous sinus injury. Most of the experiments confirmed Wittmaack's early observations. Other investigators were able to produce much the same result and for the most part gave support to Wittamaack's view.

The striking difference on comparison of the experimentally produced bone process with the otosclerotic process concerned the extent of the pathological process. Whereas the otosclerotic process is confined to circumscribed foci, restricted to definite areas of predilection, the experimentally produced process is much more diffused. However, such a difference can be explained by the uniform vascular supply in the labyrinthine capsule of the chickens as compared to the heavy bony capsule, and meager supply in man.

The cause which gives rise to the <sup>to</sup> ~~sa~~ ~~sis~~ in human otosclerosis must exert an essentially more perisitant and prolonged action than the transitory traumatic obstruction produced in the experiments.

Weber in 1930 stated, "Otosclerosis represents a definite pathological bone picture and from the features peculiar to this picture certain conclusions can be drawn as to its experimental production." There are five time phases in the development of bone.

1. Fundamental stage: that is mesenchymal tissue.
2. The stage of increase and differentiation of intercellular substance and differentiation of cells surrounding the latter.

3. The stage of nucleus formation, that is the stage of hardening of the various differentiated intercellular substances by lime impregnation, forming centers for subsequent deposition of the next stage.

4. Stage of shell, bone formation. This bone appears in the presence of osteoblasts in epithelioid arrangement. Mostly of lamellar type but as Max Mayer points out there exists a lamellar, free type within the labyrinthine capsule.

5. The stage of resorption, either directly by means of vessels or osteoclasts.

These five stages form the bone forming system. This harmonious combination within the organism comprises the bone picture.

The bone picture of an individual depends upon his age and the place from which the material is taken. Furthermore these are variances in the individual species. But for all normal healthy individuals there is a "normal bone picture."

Pathological changes of bone are expressed in alterations of the time phases of the normal bone picture. These factors may be conditioned by factors of time, place, quantity and quality.

This is the "pathological bone picture." Otosclerosis is a peculiar focal involvement of the bony labyrinthine capsule which may lead to ankylosis of the stapes, but not necessarily.

Manasse, VonRecklinghausen, O. Mayer and now Weber notice the similarity of otosclerosis with the bone picture of osteodystrophia fibrosa. Only however in the localized form. Both diseases may develop along the same course, but it is not essential for them to have the same pathogenesis in order to present the same end picture.

Both may represent a degenerative, reactive, reparative process. A dystrophy, probably through action of the blood vessels, causes degeneration of bone or cartilage, leading to irritation of the bone forming system.

This manifests itself in resorption and in the appearance of young mesenchymal tissue, which is the first stage in bone formation.

Then follows the differentiation of fibrous marrow, fibroblastic osteoid, and fibroblastic nucleus (plexus like bone). The higher unit of bone formation namely "shell bone" does not develop. Regressive changes now interfere, the maldifferentiations have been called harmatomias, by Weber.

In a hyperplastic form this particular harmat oplasis represents a pseudo tumor, with the bone picture of osteo dystrophia fibrosa. Intra-osseous epulis and "brown tumors" are remarkably similar to these pseudo-tumors.

We have mentioned the bone changes in regard to time, space, quantity, and quality. Let us now analyze the bone changes of the otosclerosis in that regard.

1. Time:

Just when the disease begins, we do not know. It may begin in utero, however, we are certain that the bone picture reaches its completion some time in the postfoetal period.

2. Concerning the element of space, otosclerosis is limited to definite locations in the labyrinthine capsule. The peculiar blood supply to these regions has great significance as to the localization.

3. Quantity:

Figure I. Reveals displacement to the left. The earlier stages of differentiation are increased in quantity. Indicating an irritation of the fundamental stage of the bone forming system and of a consequent

Normal -

M1 center of gravity of Normal

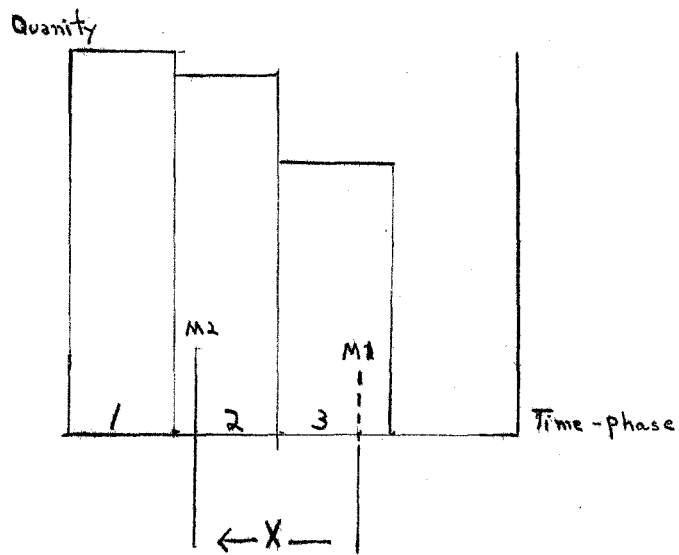
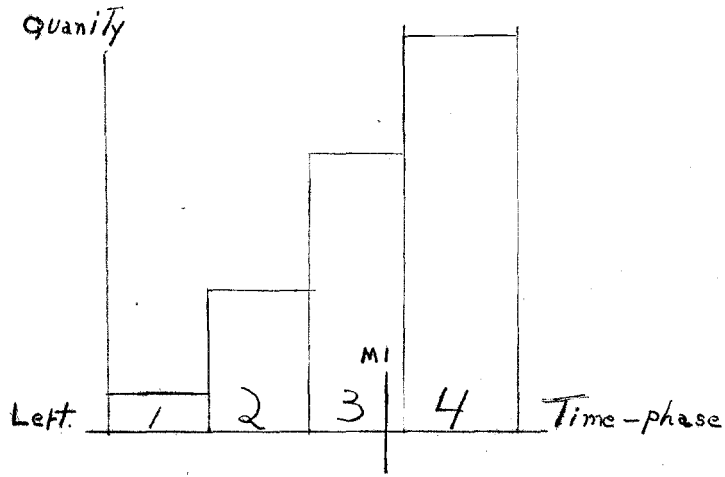


Fig. I

progression.

However, the highest unit, bone formed in the presence of osteoblasts in epithelial arrangement is absent, which might be a sign of regression.

If the total amount of apposition exceeds the limit of normal apposition with displacement to the left-- Weber speaks of "Absolute" displacement, (hyperplastic form). If the total apposition does not exceed the normal limit, he speaks of it as relative displacement.

#### 4. Quality:

Malformation as a result of a faulty differentiation of the bone forming system.

The fundamental problem then is, how can this bone picture be reproduced experimentally?

(1) according to O. Mayer, Otosclerosis is a tumor like hypertrophy a hyperplasia originating from a primarily faulty anlage. Wittmaack states that otosclerosis is the end product of dystrophy caused by venous stasis.

While Weber takes the intermediate road, regarding otosclerosis as a pseudo tumor, resulting from a maldifferentiation, which may originate from a faulty anlage but not of necessity. He is of the opinion that a secondary dystrophic disturbance, appearing very early, may lead to the same morphological end-picture as a primarily faulty anlage.

Since the possibility of experimentally producing otosclerosis from a primary faulty anlage is still remote, the author chose the possibility of the synthesis of the bone picture of otosclerosis, by a secondary dystrophy.

Principle postulate.

(1) An irritation of the bone forming system must be produced, which attacks the areas of predilection to a local progression.

Progression must be arrested and a tendency to faulty differentiation be produced.

What are the possibilities for fulfilling the above?

Not infrequently, otosclerosis appears either in connection with osteogenesis imperfecta with generalized osteodystrophia fibrosa. Assuming that the bone picture of these diseases can be produced experimentally.

1. Osteodystrophia can be produced by disturbances in metabolism, Dr. A. F. Morgan and Dr. H. Beck producing the disease in dogs by a purified diet low in calcium and completely lacking in vitamin D. How might the bone picture of otosclerosis be superimposed upon such an experimental result?

In the experiments otosclerosis probably did not occur because cartilaginous remnants had already disappeared by the time the diet was begun. However typical osteodystrophia fibrosa was produced in the epiphyseal line of the long bones. Therefore if such remnants had been present in the labyrinthine capsule it would be the first to suffer dystrophy, with regeneration and resorption.

The break down products leading to a local irritation giving rise to a pseudo tumor. Thus producing otosclerosis as a pseudo tumor in generalized Von Recklinghausen's disease.

Experimental production of osteogenesis imperfecta. The bone picture of this disease shows a relative displacement to the left. The condition seems to be the result of intra uterine scurvy. The prevailing theory however being that the disease as a generalized faulty anlage of the entire supporting tissue of the body. However why not produce the same end result by producing scurvy. The bone picture must be the same, for in scurvy as in osteogenesis imperfecta a pseudo tumor appears in the vicinity of fractures and hemorrhages.



Therefore in order to produce otosclerosis in intra uterine scurvy, providing cartilaginous remnants are present one must have some form of irritation. Venous stasis according to Wittmaack seems well adopted to this.

This time producing otosclerosis as a pseudo ~~tumor~~ in osteogenesis imperfecta.

It is questionable whether or not otosclerosis can be produced without some accompanying disturbance of metabolism for Biochemistry has taught us that all cases of otosclerosis are accompanied by a generalized disturbance in metabolism. However, these disturbances may not have the same biochemical aspects.

## INFLUENCE OF GENERAL CONDITIONS

Again we must refer to the early writings of Toynbee, who in 1857 advanced the theory that stapes ankylosis was a form of "rheumatic gout" of the stapedio-vestibular point. His theory is immensely interesting. Gout, he states, is associated with an excess of albumin in the blood and involves vesicular tissue. Rheumatism is associated with an excess of fibrin in the blood and involves, fibrous tissue, muscle fibers, tendons, synovial and other serous membranes.

Rheumatic gout affects both fibrous and vesicular structures and consequently the stapedio-vestibular joint. Toynbee pointed out that patients with rheumatic gout of the stapedio-vestibular joint usually showed uric acid diathesis.

Erhard noted that this form of deafness was more common in women who had had children, there being a decreased activity in the hearing following each pregnancy. He also noticed that this form of deafness was more common in women than in men, and that the majority of his patients resided near the sea shore and that the advance of the process was favored by cold.

Gradenigo in 1893 found that the disease is seriously aggravated by each pregnancy and the puerperium so that each

child birth is followed by a definite diminution of hearing.

In both sexes conditions are usually found that indicate vascular irritability, that is rise of blood to the head, vertigo, circulatory disturbances, edema etc.

Later the same author stated that he had studied a new series of sclerotic otitis based on hereditary syphilis. Regarding the sclerosis as an attenuated form of the ear disease of hereditary syphilis of Hutchinson. "Every case of progressive deafness developing in a young person without a history of hereditary deafness or tuberculosis should be regarded as suspicious or syphilis."

One of the most complete studies was done by Helot in 1900 in which he examined 885 pregnant women. Finding that in some cases the hearing was diminished during pregnancy, but returns to normal after delivery. However he states that these cases should not be confused with those cases of middle ear sclerosis in which a permanent diminution of hearing follows pregnancy and becomes worse following delivery, in other cases hearing may be normal before pregnancy. Should there be several pregnancies at short intervals with long periods of lactation, there seems to be a marked progression in deafness if sclerosis is present.

The author's opinion as to the cause of sclerosis following pregnancy is: that during pregnancy there is a congestion of the Eustachian tube and middle ear that is sufficiently prolonged to cause changes in the structure of the mucosa, with proliferation of connective tissue which becomes fibrotic and which results in compression of the nerve fibers producing a trophic lesion terminating in a sclerosis of the tympanic cavity.

Dicke in 1903 goes back to Toynbee's original theory and believes that the condition is a uric acid toxemia, attacking the individual at his "most vulnerable point, the labyrinth."

Downer at the same time expressed the opinion that in otosclerosis the patient will be found to be a "quinine devotee." Quinine, he claims, produces intense congestion of a long lasting type which grafted on the uric acid or catarrhal type leads to a chronic condition.

Haberman in 1903 becomes quite radical and believes the cause of otosclerosis to be specific and regards syphilis as the cause. In his series of 30 cases, 5 were definitely syphilitic and syphilis though not demonstrated could not be excluded in the others.

Another factor suggestive of syphilis is the onset of otosclerosis during the twentieth to fiftieth year of life, the time when syphilis is most commonly acquired. Likewise the histological findings in the bone are quite in accord with the histological findings in syphilis.

However several investigators can not agree with Haberman's view and produce rather conclusive evidence to support their view point.

In view of the wide spread incidence of syphilis, fixation of the stapes would occur much more frequently than it does as a secondary condition.

The incidence of syphilis is highest in men, that of otosclerosis in women. Syphilis has been excluded definitely in a large number of cases studied by Denker.

Cornet in 1908 in a very interesting study of 19 cases was able to make a complete examination

of 18 of the cases. Of these 8 were elderly patients of arterio-sclerosis or high blood pressure. Of the 10 remaining there were, one renal insufficiency and alcoholism, one hepatic insufficiency, two dyspepsia with gastro-intestinal atony, four gastro intestinal disturbances of various types with toxemia shown by etheral sulphates in the urine. One case had repeated pregnancies in addition to gastro intestinal toxemia.

The author's conclusions, though unable to definitely establish gastro intestinal toxemia as an etiological factor in otosclerosis, do give some support to this hypothesis.

1. Its hereditary character, for the toxemias are also hereditary and probably act upon the auditory organ rendered vulnerable by hereditary conditions.
2. Its insidious development in young subjects in whom chronic toxemias are often latent.
3. Its frequent development at the time of pregnancy which results in special modifications of metabolism.

Ferreri in 1910 made the statement that the theory that otosclerosis is due to auto intoxication has gained ground. In certain counties in England and Italy where gout and gouty diathesis are frequent otosclerosis is also frequent.

The majority of cases of otosclerosis observed in gout are not due to gout but to a metabolic failure. Such auto intoxications are hereditary and latent so that otosclerosis does not occur until a period of special strain on the organism.

He believes that the cause is attributable to circumstances that affect the general nervous system or the alterations of the normal condition of the blood and circulatory system.

Tweedie in 1908 is convinced that otosclerosis is not catarrhal in origin nor is it due to any inflammatory cause nor does it originate in the middle ear.

He believes that the cause is attributable to circumstances that affect the general nervous system or to alterations of the normal condition of the blood and circulatory system.

The author refers its onset to sudden grief, shock, fright, prolonged mental anxiety, affecting the general nervous system: or it may be associated with chlorosis, anemia, severe hemorrhage and parturition. General febrile conditions especially influenza may be associated with the onset.

Heiman in 1909 believes that a very common factor in the etiology of otosclerosis is represented by anemia and chlorosis. He noted that in his series of cases thirty-five per cent could be traced to these conditions. Anemia seems to be a positive factor exclusive in women. Perhaps a certain part is played by menstruation which temporarily increases the anemia, and also temporarily induces congestion of the head.

Pregnancy was found to be a factor in six per cent of the author's patients. Here again the otosclerosis is the result of some change in the blood which exerts a deleterious influence upon the organ of hearing in particular.

Bryant in 1913 came to the conclusion that the pathological changes noted in otosclerosis were the exact counter parts of other non-suppurative processes in the bone elsewhere in the body. For example, osteitis, rachitis, osteomalacia, syphilis, tuberculosis arthritis, deformans, osteitis fibrosa, etc.

He holds that otosclerosis is a dystrophic process related to osteomalacia.

The author believes the causes to be manifold in character differing in no way from the causes of other non-suppurative bone lesions outside the temporal bone. He is among the first to mention possible endocrine dyscrasia as a likely etiological factor. Likewise he again mentions trophic and toxic causes and believes the hereditary factor lies in a diminished resistance of the autonomous and sympathetic nervous system.

Mayer points out that the disease is characterized by proliferation of the fibrous marrow and therefore resembles the disease described by Recklinghausen. Moreover Mayer states that the disease is due to local circulatory described disturbances, and therefore agrees with the etiological factor described by Recklinghausen as being the result of irritation to vasomotor nerves leading to repeated congestion of the bone marrow.

Aside from functional disturbances, organic changes in the blood vessels may also be a basis for sclerotic changes. Autopsy findings show arteriosclerosis to be an accompaniment of otosclerosis in many cases. Therefore such general diseases causing arteriosclerosis may also cause otosclerosis, that is, scarlet fever, typhoid, diphtheria and influenza.

To more thoroughly establish his theory the author presents a case of Recklinhausen's osteitis localized in the skull who was hard of hearing. The patient had eight children and four abortions and for three years had noticed an increase in the size of the head, pains in the occiput and increasing deafness. The Xray examination shows typical changes of Recklinghausen's disease in the skull.

the hearing test though not definitely showing otosclerotic changes could not definitely exclude the presence of osteitis fibrosa of the labyrinthine capsule.

Denker in 1912 believes in the heredity disposition to the disease. The predisposition being the foundation upon which the disease arises under influence of certain irritants. Among those irritants are: increased bone formation during puberty, bony changes during pregnancy and circulatory disturbances such as are present in arteriosclerosis, vasomotor neuritis and syphilis.

Two years later the same author enlarged upon his theory of hypophyseal changes. It is well known that dysfunction of hyperfunction of the hypophysis may cause bone changes, as in acromegaly. Though the bone changes of otosclerosis are not comparable to those of acromegaly the frequent onset of otosclerosis during pregnancy concomittant with changes in the hypophysis is suggestive of an etiological factor. To further his studies Denker employed Abderhalden's dialysis test for protective ferments against hypophyseal products in the blood of twenty-two otosclerotic cases and thirteen control cases. Of the twenty-two cases of otosclerosis seven teen showed anti-hypophyseal ferments while control cases showed only four.

In 1914 Bauer and Stein in a most exhausting study of the constitutional factor in the etiology of otosclerosis studied twenty-six cases, eighteen women eight men. The following is the list of symptoms supposed to be indicative of an abnormal constitution, arranged in order of frequency.

Anomalies of the vasomotors (dermographism of variable intensity.) Lability of heart action, as well as respiratory



irregularity of pulse, Aschners bulb pressure reflex (retardation of the pulse by pressure upon closed eye balls), Erbens pulse phenomena (retardation of pulse by flexion of legs or stooping.)

Exaggerated tendon and periostial reflexes, lateral differences in reflexes of the abdomen, the left being weaker than the right or entirely absent. Anomalies of sexual function, premature or delayed onset of menstruation, irregularity of menstruation, dysmenonhea, hypoplastic genitals, anomalies in the hairy covering of the trunk (female type of pubic hair in men- male type in women), absence of axillary hairs, anomalies in the size of the breast or nipples, hyperplasia of the lymphatic pharyngeal ring and many other signs and symptoms to numerous to be listed in full.

The explanation of such an amazing amount of material had probably best be done in the author's own words. "Probably there hardly exists a person free from one or another of the symptoms, without any indication of disease being present." The note worthy feature in the cases examined by the author is the large number of stigmata found in the same individual. The constant occurrence of these degenerative signs in patients suffering from otosclerosis indicates a hereditary degenerative disposition of these patients and explain the abnormal reaction of the organism of such persons toward irritants of all kinds."

The cumulation of degenerative signs, observed by the authors, with otosclerosis is thought to exclude accidental coincidence.

One symptom demonstrable in all cases of otosclerosis is lability of circulation which has its origin in hyperirritability of the vasomotors and lability of the heart action. Therefore the possibility mentioned by Mayer must be borne in mind and the lability of the vasomotors should be credited with special significance in the origin of otosclerosis.

After a brief summary of age and sex incidence, heredity and course of otocloserosis and arthritis deformans, O'Malley concludes that:

Chronic adhesive process of the ear is a rheumatoid arthritis affecting the organ of hearing.

The two diseases are frequently associated in the same individual and occurrence of osteoarthritis in the female progenitors of many of the subjects of otosclerosis have been noted. Developmentally, anatomically and physiologically, the affected structures are all alike, considering then identical types of destructive and reparative changes occurring in these similar structures, the inference would be that the processes are the result of a common pathogenesis.

Further similarity lies in the two conditions, for example, there is a striking analogy between the two diseases in age, sex, race, and hereditary incidence, symmetry of lesion, trophic changes, cause, associated diseases and conditions said to influence onset and exacerbations. Two outstanding features run side by side throughout the whole process, hypertrophy and atrophy.

In 1917 a valuable contribution was added to the work being done in the field of otosclerosis. At this time Frey and Orzechowski found that in latent tetany there was frequently associated deafness. In five unselected cases of otosclerosis they were able to show definite evidence of latent tetany, in three cases and in the other two, less definite symptoms of latent tetany.

The authors then note the following characteristics of otosclerosis, and conclude from them that otosclerosis is not merely a biological process but is dependant upon general changes in the organism:

1. Family heredity, important.
2. Bilateral occurrence almost exclusively.

3. Frequent beginning of the process soon after puberty second or third decade at the least.
4. Frequent onset of the process in women during pregnancy or immediately after delivery, aggravation of otosclerosis by pregnancy.
5. Frequent presence of various vasomotor disturbances.
6. Occurrence or aggravation after gave psychic trauma.
7. Peculiar body type of otosclerotic, not yet analyzed, but definite enough in that many otologists recognize otosclerosis before examination.

In 1920 the same authors reported ten additional cases of otosclerosis examined for latent tetany. Of these ten cases, five showed evidence of latent tetany, four, less definite evidence, but a probable diagnosis of tetany could readily be made, the last case showed no signs but was not examined completely.

At the same time Roch studied eighteen cases of otosclerosis for tetany and failed to elicit a symptom suggestive of the disease. He concluded therefore that Frey and Orzechowski used patients coming from tetany districts.

Frey, in responding to Roch's criticism of his work, notes that the patients studied by him were not of a limited territory but were soldiers from various regions of Austria-Hungary.

He then makes the statement, "Should the foregoing experiences on the occurrence of latent tetany in otosclerosis be confirmed in a larger material, a possible, perhaps complicated, dependence of otosclerosis on latent tetany, namely parathyroid insufficiency would have to be taken into consideration.

Throughout the literature constant reference is made to the association of otosclerotics and blue sclerotics.

Fraser, probably gives us the most likely explanation. He notes

that fragilitas ossium has been attributed to hereditary inferiority of the mesenchyme, the labyrinthine capsule is a mesenchymal structure. Through the association of otosclerosis with defects of mesenchymatous structures seems to be of importance Fraser does not believe that otosclerosis can be entirely explained this way. He believes there is too great a tendency to try to link otosclerosis with a single cause, while it seems more probable that it is a result of several causes combined. Heredity, endocrine dysfunction, toxemias and loss of nerve influence are all important, he declares. His conclusions are: that an attack of otitis media may be compared to "the match that fires the magazine", hereditary tendency corresponds to the "powder", the loss of nerve influence and disorders of the ductless glands compared to a "want of water with which to extinguish the flames."

Pratt in 1919 is convinced that ductless gland dysfunction is the underlying etiological factor. Since the hypophysis and adrenals influence bone growth he believes that these two glands are chiefly responsible.

Callison 1921 found that otosclerotic patients showed evidence of glandular deficiency as measured by conditions of the skin, hair, lability of cardio vascular system, etc. There is some increase in the elimination of both calcium and phosphorous in the urine.

He includes in those glands responsible, those glands that control calcium metabolism and those that control the oxidation of the body, first is the thyroid, which not only controls cellular metabolism, but calcium and phosphorous metabolism as well, combined with the thyroid are the interstitial cells of the sex glands. Since definite proof of their effect upon bony changes has been proven by changes in castrated animals. The influence of the parathyroid, thymus, pituitary and

suprarenals is still problematical.

Escat disregards all theories excepting that of endocrine dysfunction. He mentions the interrelationship of the endocrine glands and importance played by the ovaries in the female sex. The progress of the disease process is accelerated at two poles of sexual life, puberty and the menopause, it is also accelerated by pregnancy and lactation. When the menopause is over the process is arrested.

To support his contention he reports the following case: A woman thirty-two years of age, in whom a total hysterectomy was performed was followed not only by the arrest, but by partial regression of typical otosclerosis with ankylosis of the stapes.

In 1922 Kauffman points out the similarity of the bone changes in the temporal bone in rickets, and otosclerosis. Rickets is a deficiency disease. He therefore forms the hypothesis that it seems reasonable that a similar deficiency acting throughout different periods of life may produce not infantile rickets, but bony changes, elsewhere, as in otosclerosis.

Working on this supposition Kauffman and his associates, made experiments on young rats fed on two types of deficiency diets. The rats were killed at the end of three months and a study made of the labyrinthine capsule.

It will suffice here to state that they found changes in the temporal bone entirely analogous to those in the long bones. Since other investigators have demonstrated that healing processes take place in the long bones in experimental rickets the authors believe it is possible that similar healing processes would take place in the temporal bones and give a picture identical with that in advanced otosclerosis. Indicating that otosclerosis may be a result of rickets or a dietary deficiency similar to that which causes, rickets, still

existent during adult life.

In 1922 the study of blood chemistry again leads the field of investigation. At that time Leicher reported the determination of the calcium content of the blood serum in thirty-two cases of otosclerosis. In twenty-four cases the calcium was found to be diminished below the normal limits of variation. Six of the eight cases with apparently normal figures showed evidence of abnormal calcium metabolism as shown by the fact that after administration of primary sodium phosphate for two weeks, there was a definite lowering of the calcium content of the serum, whereas twenty normal persons under the same conditions showed no change. In the remaining two cases the test could not be made. In view of the periodicity of the remissions and exacerbations in otosclerosis one might expect to find normal blood calcium at times. The diminished calcium ions leads to an increased neuromuscular irritability which manifests itself in the symptoms of tetany.

For an etiological explanation of these findings the author turns to the endocrine glands.

The author's summary is as follows:

1. The calcium content of the blood serum in 70-80 per cent of otosclerosis patients is definitely diminished.
2. In apparently normal otosclerotic patients the blood demonstrates a lability upon the administration of primary sodium phosphate.
3. The determination of calcium content in the spinal fluid of two patients showed normal values.
4. Clinically this calcium deficiency may manifest itself by (a) the phenomena of Chvostek, Erb, Trousseau; (b) by disturbances on the part of the vegetative nervous system (nervous gastrointestinal disturbances,)

circulatory irregularities (disturbances of heat regulation).

5. The cause is presumably endocrine or constitutional anomalies.

In 1924 Drury reported forty-four cases of otosclerosis studied specifically for endocrine disturbances. The basal metabolic rate, vital capacity alveolar C O, blood chemistry, blood counts, urine chemistry and sugar tolerance were determined, and special eye, neurological and ~~roentgen~~ studies made. Sixteen cases showed no evidence of glandular dysfunction; two were syphilitic, twenty-six had evidence of glandular dysfunction; nine of these showed pituitary dysfunction, six gonad dysfunction, three thyroid dysfunction, in eight the gland could not be determined. From these series of cases the author concludes that the endocrines are important etiologically and that the findings indicated a lowered rather than an increased glandular function.

Manasse, who made exhaustive studies of the cholesterol content of the blood, concludes that the deposit of cholesterol not only depends upon the hypercholesterolemia but upon local tissue conditions. Though he reports both a hypo and hypercholesterolemia in these cases, the latter seems concomittant with pregnancy.

He believes the cause of the metabolic cholesterol disturbance is endocrine in origin.

Stern in 1926 reported the effect of the blood serum of patients with otosclerosis on the growth of seedlings of *Lupinus Albus*. In twenty cases the seedlings not only showed definite inhibition of growth but also evidence of atrophy as compared to normal serum.

Leicher later extended the work of Stern and reported not only the serum exerted a toxic effect on vegetable cells but also to a lesser degree, the urine, the saliva and the sweat of otosclerotics.

This toxic substance was demonstrable in the alcohol, chloroform, ether, and acetone extracts of these body fluids. The author considers,

the phosphatides as being the probable vehicles of the toxin.

Werner states that Bock has described a polarization method for the demonstration of hormones in the blood, no hormone being found in the blood of normal persons. Using Bock's method in his study of twelve cases, Werner was able to demonstrate the presence of several hormones.

However a variety of combinations were present, Thyroid, ovarian, pituitary, suprarenal and pancreatic were found. In three fourths of the cases parathormone was demonstrated.

The survey of the material available for the year 1929, first mentions Harris's study of eight-two cases with no history of suppuration. The method of selecting these cases was to select cases of gradually progressive deafness, with no history of suppuration and no thought of the morbid anatomy. Each case was submitted to in addition to the hearing tests, complete physical examination and blood studies.

A family history was found in only eight per cent of the cases.

The drum membrane was normal in a great majority of the cases. Sixty three showed a raising of the lower tone limit. In forty six bone conduction was length end and normal in twenty but these were cases of only short duration. Rinne's test negative in fifty one and positive in fourteen. The auditory tube was normally patent in all cases. These observations are at variance with many writers view points, notably Bezold and Eneerson.

The audio grams were divided into four classes,

1. Those showing a loss mainly at the lower end of the scale.
2. General lowering of acuity.
3. Lowering at both ends of the scale.
4. Lowering at the upper end. Analysis of the graphs showed an approx-



imately uniform reduction of the hearing over the entire scale in forty-one cases: twenty five cases showing a lowering chiefly at the upper end. Based on relationship to the duration of deafness, about one half of the cases in which the upper limit was involved had lasted less than three years. A little over half of those showing uniform reduction were also less than three years duration.

All cases were investigated for focal infection. Only fourteen cases of diseased tonsils, three sinusitis and a few others of miscellaneous sources were found.

The urine was normal excepting for one case of diabetes, four positive Wassermans and Kahns were found all in women who did not show severe deafness. The blood calcium was above normal in three fourths and below in ten. In thirty seven cases the uric acid was above normal. The Basal Metabolic Rate was above normal in twenty three cases. Thirty nine were examined for endocrine disturbances, thirty four showed some abnormality. Thirty five were married women, in eleven the deafness began after child birth, in eight it was worse after partuition and in nine it was present before marriage.

Willige and Loebell were among the first investigators to analyze the affect of pregnancy upon women with normal hearing. Willige examined thirty five women in the 6-10 month of pregnancy with reference to their hearing. The majority of the patients had large collection of wax, and arcus cypoid in the cornea and ear drum and a slight degree of inner ear deafness.

The latter showed itself by shortened bone conduction and lowering of the upper limit and the monochoid. Seventeen of these were examined from 6-10 days after partuition. In all cases the upper tone limit was again normal but the bone conduction was still shorted in about one-third.

Other authors have shown an increase of cholesterol in the blood during pregnancy.

Loebells, series of 151 women examined in the last trimester of pregnancy showed that 60 per cent showed a diminution of hearing of the perceptive type.

The Rinne test was positive and the lower tone limit normal in all cases. The upper tone limit was 20,000 in all but 2 cases. Bone conduction was diminished for C and for C 5. Only four showed improvement postpartum. As most of these patients were unmarried women who had repeatedly been examined in the maternity clinic, Loebell believed that there was a large psychologic factor in his cases.

Gottlieb studied thirteen cases of progressive deafness. A noteworthy feature was that the results of hearing tests varied from time to time, indicating one examination is not enough to gain a true picture of the condition. Such changes suggested to the author that perhaps hearing defects were not due to changes in the osseous labyrinth but to alternate laying down and absorption of exudates in the membranous cochlea.

Six cases showed contraction of the color fields and in four of these heredity was a factor. Concomitant abnormalities were present in all cases. In three cases the uric acid content was abnormal and the calcium in four.

Gottlieb then carried out a series of experiments in which extracts were made from the feces of patients suffering from progressive deafness. These extracts were injected into guinea pigs. The same was done with extracts obtained from persons of normal hearing. Hemorrhagic lesions appeared in the inner ear of those guinea pigs injected with extracts from patients, but not in the others.

Drury presented a study of 10,000 cases histories bearing on the relation of endocrine glands to deafness. Deafness was a presenting symptom in eighteen per cent of the cases of thyroid disease, in twenty two per cent of those of pituitary disease and in thirteen per cent of those ovarian disease. The largest proportion showed diminished function of the gland in question. Administration of the gland produced considerable improvement both in general health and hearing of patients with thyroid or pituitary disease. Results of ovarian glandular therapy were disappointing.

Behrendt and Berbrich compared the blood chemistry of rickets and otosclerosis. The changes corresponded in some respects. The alkali reserve of the blood was lowered, but the acid secretion of the urine normal. Therefore the characteristic feature of rickets, viz, hypophosphatemia, was absent. Therefore they concluded that in otosclerosis there are disturbances of metabolism, of intermediate degree, which in many ways are analogous to those in rickets.

Josephson states that there is a characteristic and constant injection of the vessels of the drum and the inner end of the external auditory meatus. He leaned to Wittmaack's view of vascular stress on the observations of Gray that vaso dilators, nitrites, will temporarily improve hearing. In this test he suggested a means of determining prognosis. Since if a patient responds to vasodilators irreparable damage has probably not occurred as yet.

Harris reports out of 60 records of otosclerotic patients fourteen cases of women where the history was one of not or comparatively slight deafness until the first or subsequent pregnancies, when almost in a moment the hearing became seriously affected. Encouragement is lacking in such cases that in time the hearing might be improved. Many leaders in the progression suggest that if pregnancy

occurs in these cases, an interruption is the proper course to be carried out.

Various explanations have been advanced for this affect of pregnancy. Neuman thinks it is due to lowering of the bone resistance, Cornett to auto intoxication, Otto Mayer to otosclerotic areas in the pregnant woman. Alexander thinks the bone changes to be of a congenital nature.

Stein's opinion is that there is a constitutional diminishing of the hearing due to developmental anomalies in the labyrinthine capsule, there being a predisposition to otosclerosis on the one hand, and on the other, to atrophy of the nervous apparatus.

Mirvish "29" worked chiefly with parathormone treatment in cases of otosclerosis, however his work seems valuable from an etiological stand point. We have seen the general trend to the study of endocrine dysfunction in the more recent literature. Otosclerosis is a disease of the bone. The endocrine glands especially the parathyroids are known to influence the calcium metabolism and through it bone growth, further investigation has demonstrated that the concentration of calcium in the blood is below normal in otosclerosis such as one would expect in hypoparathyroidism. Other evidence pointing in the same direction is the frequent occurrence of latent tetany in otosclerotic patients and manifest tetany during pregnancy. On this basis Mervish began his work in the treatment of otosclerosis with parathormone. No attempt will be made here to a detail review of his work. The work represented an intensive study of a few cases of otosclerosis who were treated with parathormone injections, and whose hearing was continuously controlled by quantitative hearing tests.

The number of cases was of necessity small but observations of one to three years justified certain conclusions.

In the cases reported parathormone definitely arrested the progress and improved the hearing in two cases. The improvement was manifest in the first two months and progressed no further. On the other hand the improvement was maintained all the time. The author suggests that otosclerosis is analogous to osteomalacia and rickets, and that these three metabolic diseases have as a basis of their pathology a common factor, hypoparathyroidism.

Warrick in 1931 believed that progressive deafness is caused by the intermittent although infinitesimal deposition of mineral salts about the foot plate of the stapes and the margin of the oval window eventually resulting in interference of normal vibration of the stapes in the fenestra ovalis.

He notes that the mineral constituents found deposited in otitic senility are composed of calcium carbonate and tricalcium phosphate. These are two principal constituents of normal bone. Serum contains calcium and organic phosphorus in a solution in much higher concentration than would be possible in water on account of the high carbon dioxide tension and the colloid contained in the serum. When the concentration of calcium and phosphorous reaches a certain point, a decrease of CO<sub>2</sub> tension which increases the alkalinity brings about the precipitation of the tricalcium phosphate. Therefore in dead or inactive tissue CO<sub>2</sub> tension is low and conditions are favorable for precipitation.

The possibility of the presence of a calcium binding substance within the area is an attractive one. Cartilage is one such substance.

Wells found that certain substances when introduced into the tissue had far greater powers of calcium absorption than others.

For example fat, spleen, thymus are found to contain 12m. gm of calcium after a stay of fourteen weeks in peritoneum where as a similar piece of cartilage has absorbed 15-4m gm even after being devitalized by boiling.

If we recall Mayer's work on otosclerotic foci we can readily see the excellent opportunity of calcium deposition in these areas.

In considering some of the circumstances which alter calcium metabolism Warwick believes that there is too great a tendency to the belief that pregnancy and ovarian disorders were invariable concurrent with otosclerosis.

The author upholds Fraser's view that otosclerosis may be due to a multiplicity of causes.

Observing his own patients the author noted that a number gave a history of having been weaned from the breast and fed on sweetened condensed milk. Investigators have shown that condensed milk is deficient in vitamins A and D. Investigators producing symptoms of bone disease, rickets with a diet of condensed milk fed to rats. Moreover mothers fed on a vitamin deficient diet give birth to poorly developed children. From this observation he concludes, that the hereditary tendency of otosclerosis results in a deficiency in formation of the temporal bone in the fetus and early months of infancy. That the cartilage cells become sensitized in such a nature that <sup>in</sup> adult life they become responsive to changes in the hydrogen ion concentration of the blood, and of blood calcium, such as occurs temporarily during the endocrine deficiency of lactation.

In view of the fact that all physiological and pathological variations are intimately connected with calcium metabolism,

and otosclerosis is a variation in bony growth it would seem logical to search for blood calcium and phosphorus variation in this disease.

One endogenous store of calcium is bone. Phosphorus is available in all tissues in the form of phosphoric acid. Calcium metabolism consists of: diet as the supply, upper intestine as the absorber, the serum as the carrier, bone as the storehouse and the kidney and lower intestine as the eliminators.

The factors influencing absorption are:

1. The amount of calcium.
2. The acidity of the food.
3. The amount of available fatty acids.
4. The presence of vitamin D.

The factors influencing excretion are:

1. There is very little conservation of calcium in the body, and excretion is on at a certain high minimum level under all conditions (Peters H. C.)
2. Excretion is raised by excess and lowered by insufficiency in (a) acid (b) parathyroid (c) thyroid activity.

The above favors depletion of calcium from bones, for calcium is a fixed base easily available. Calcium is present in blood as a complex phosphate and a proteinate. The calcium proteinate is not available, since it is more soluble in serum than in water and less soluble in intra cellular fluids, and precipitates in low protein.

Popular theories as to why calcium is precipitated are:

1. Calcium is already present and is precipitated from hypothetical supersaturated solution.
2. The removal of phosphorus by certain cells precipitates calcium.

3. Certain cells, especially cartilage have specific attraction for calcium.
4. Local changes occur in the P.H.
5. Dead and autolized bone is the source of calcium (fracture healing.)
6. Enzymes are present that precipitate calcium by catalysis and locally changing the P. H. The last three are the more plausible.

Fowler, examined all his patients' blood for variations in cholesterol few cases showed any. Fifty-eight cases had calcium phosphorous and protein determinations and showed very slight variations from normal. However all the cases were established otosclerosis.

As to incipient otosclerosis something of importance may be found. However how can we diagnose incipient otosclerosis and institute calcium therapy except vaguely by a positive family history?



## SUMMARY AND CONCLUSION

Up to the time of Toynbee 1851 the history of otosclerosis consisted of little more than fragmentary bits of anatomy and physiology, some correct and some incorrect but all furnishing a basis for further study. Toynbee in his description of the signs and symptoms and various pathological findings varies very little from the present conception of the condition. From the time of his first theory of "rheumatoid arthritis" as being the cause of stapes ankylosis many theories have been evolved.

At the present time there are probably seven main theories as to the etiology of otosclerosis.

1. Heredity, which seems to be regarded as the one constant factor in its etiology.
2. Infectious theory, more in the discard, though some otologists advise removal of all foci of infection.
3. Toxic theory, gastro, intestinal autointoxication, gouty diathesis, and a uric acid diathesis.
4. Deficiency theory, a question of vitamins, brings out analogies to rickets, osteomalacia, arthritis deformans and similar conditions.

5. Endocrine theory, more recent, received its impetus from the observed evidence of deafness and latent tetany.
6. The circulatory stagnation theory, states that a failure of local blood supply results in the absorption of normal bone and cartilage and results in spongy bone and later a deposition of lime salts.
7. The neoplastic theory, states that because of a faulty anlage with or without an exciting cause, lesions which are essentially new growths develop in a highly complex embryological portion of the labyrinth capsule.

Four theories seem to have captured most of the interest in the last few years. These theories have been discussed previously. Fowler in 1932 summarizes them so concisely and clearly that it would seem advisable to become better acquainted with their meaning.

The theory of Gustav Bruhl is as follows:

1. Osseous ankylosis, of the stapes and clinical otosclerosis are identical.
2. Before proper investigation can be made more cases of ankylosis of the stapes diagnosed in vivo should be studied.
3. Otosclerosis is a constitutionally conditioned hereditary affection, a degeneration or atavism, but not a disease. To look for the cause of the disease is hopeless.
4. Classification of all departures from normal labyrinthine bone structure as otosclerosis is wrong.
5. The bony form leading to ankylosis of the stapes consists of spongelike bone starting from the spaces surrounding the periosteal blood vessels of the vestibular window.

Irritation causes resorption of old bone and replacement by new bone. This new bone is formed in excess and is called tumor like bone.

The irritations of movement where the foot plate moves farthest and the pull of the tensor tympani in the opposite direction is thought to be a factor in the production of otosclerosis. The stress and strain of pulling and the irritation of the hyperostosis together are in his opinion the important factors.

Professor Wittmaack believes that venous stasis causes otosclerosis. He bases his theories on observations observed in a similar disease, which he was able to produce in the labyrinthine capsule of chicken by venous stasis. By thrombosing the sinus which drains the capsule of the hen with concentrated corn chloride produces a disturbance in the bone which he believes is identical with that found in otosclerosis.

Dr. M. Weber is of the opinion that otosclerosis may be regarded as a localized osteitis fibrosa. He has produced these lesions by feeding dogs on a low calcium diet with no vitamin D. He believes that the same condition is produced by venous stasis.

Mayer studied thirty temporal bones of congenital deafmutism and found in these bones typical foci of otosclerosis, moreover in otosclerosis the same changes were found as in deafmutism only to a lesser degree. In examining these temporal bones, Mayer found fissures which resembled those he had found in Pagets disease and which he termed spontaneous fractures. He has found these fissures in sixty temporal bones. These fissures are not empty but filled with fibers, poor in cells and partly ossified.

Spontaneous fractures probably were found in old pyramids. The spontaneous fractures probably have no direct bearing on otosclerosis. But the same mechanical strain occurring in the young could cause otosclerosis, since both occur in those areas in which greatest strain occurs.

#### CONCLUSION

Bruhl believes that otosclerosis is caused by irritation of the several factors working at the otosclerotic corner.

Mayer argues, if it were new bone formation that truly is the result of the mechanical irritation from the annular ligament one would expect new bone formation to begin in the cartilage layer. Mayer possesses four temporal bones all having normal cartilage layers.

Moreover the contraction of the tensor tympani muscle cannot irritate this area of predilection as the muscle has no relation to this area. The tendon passes around the cochleariformis, which should be the irritated point but shows no otosclerotic changes.

It is quite possible that in the case of the annular ligament and the tensor tympani the irritation may be transmitted. Bruhl claiming only that the constant irritations may be sufficient to cause otosclerotic changes in a susceptible individual.

Wittmaack believes otosclerosis to be caused by venous stasis. In criticism to this theory we might suggest as Guggenheim points out.

1. That the structure of the hens capsule is different than that of the human.

2. That experimentally produced condition is always generalized as to the capsule where as in the human it occurs at certain sites of predilection.
3. That enlarged vessels are physiologic in active bone changes and do not necessarily point to venous stasis in otosclerosis.
4. That Wittmaack has failed to produce any bone changes in monkeys.

Finally Wittmaack states "In spite of this knowledge, the problem of otosclerosis is not solved. The question now arises as to what causes the venous stasis."

Weber finds it identical with osteitis fibrosa and puts it on a local metabolic basis.

Weber worked in Wittmaack's laboratory and is therefore in accord with some of his views. Unlike Wittmaack he believes a great deal may be gleaned from the study of allied bone conditions. Likewise he has shown that all bone in otosclerosis is new formed bone which is a point greatly discussed by otologists whenever the histology of otosclerosis is considered.

Weber admits he does not know what causes otosclerosis, but unlike most investigators has entered the problem with a broad scientific attack that should prove valuable.

Mayer believes the condition to be the result of a profound strain, the nature of which is undetermined, but the presence of which he proves by the finding of fractures in the sites of predilection for the disease.

Guggenheim says of Mayer's theory, "This may well be true, but Mayer's observations while scientifically of great interest, do not reveal, the otosclerotic secret of the predisposed individual."

We have seen that heredity seems to be about the one constant factor agreed upon by those working upon the problem. That the characteristic is a recessive one seems to be fairly well established

The frequency that a hereditary factor occurs in the condition is a much disputed question. Many so called family histories may prove negative upon closer investigation. A deaf grandparent may have been deaf from an injury. The diagnosis of otosclerosis may not have been made in other deaf members of a family. Nash in 1930 studied one thousand cases of otosclerosis, and less than six percent were definitely diagnosed as otosclerosis. A family history occurred in forty-eight percent.

In just what manner the condition is inherited is still unanswered. However, the work of Guggenheim in 1932 in which he attempts to prove that otosclerosis is directly the result of a regression in certain individuals through secondary mesenchymoid activity, to a lower vertebrate level, as far as the aural capsule is concerned, is very plausible, and when completely worked out should prove to be that heredity, something all investigators refer to but fail to establish. In answer to the questions asked in the introduction to this work may it be said:

The disease is hereditary. That a family history worked out especially if the patient be a woman is enough to caution her about marriage. If she is deaf pregnancy is apt to increase her deafness. If she is not deaf pregnancy is apt to prove to be the exciting cause. Marriage between two people both with family histories indicating otosclerosis is hardly permissible.

Hereditary deafness presents a rather dark prognosis. If the condition is a regression, a maldevelopment, then treatment can be of little avail. Should the condition be a hereditary predisposition, then by ruling out exciting factors, results may be obtained.

The psychic changes are immensely interesting. Whether they are part of the condition or merely the result of the condition is difficult to state. It must be admitted that with the nervous instability, and concomittant findings indicating maladjustment one would be inclined to believe they are part of the condition. However, it is said that those patients instructed in lip reading frequently show normal social trends, and lose the feeling of being a social outcast. Moreover do deaf people, deaf from some other cause possess the same outlook? If so, we must conclude that we are dealing with a condition which is the result of the loss of hearing.

At present however I am inclined to believe that the condition is just as much a part of otosclerosis as the progressive deafness and that treatment along these lines is to be recommended.

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