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JAN 17 1914A CASE OF TOTAL DEAFNESS FOLLOWING
A DOSE OF QUININE.*BY MILTON J. BALLIN, M. D.,
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It is a well recognized fact that drugs such as quinine, salicylic acid, morphine, and alcohol, when administered in one large dose, or when given in small doses for a longer period, occasionally exercise a deleterious influence upon the nerves of special sense. These drugs, owing to their toxic action, may, as I have occasionally observed, give rise to pathological conditions in one or more nerves, which partially or totally impair their function, and not infrequently prove of a temporary or permanent nature.

This applies especially to quinine, whose toxic action occasionally produces destructive changes in the terminal filaments of the auditory nerve, which appears to be particularly susceptible to the influence of this drug. The idiosyncrasy of some individuals to the effect of quinine becomes manifest even after the administration of very small doses, in that they complain of flushing of the face, headache, tinnitus of varying intensity, and more or less impairment in the hearing in one or both ears. In almost every case these manifestations disappear within a short time, leaving no harmful sequela. It happens, however, that cases are met with in which the deleterious effect of quinine makes itself apparent in pathological conditions in the labyrinthine portion of one or both ears, with the result that there is a temporary or permanent

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loss of the hearing function, with or without disturbances in coordination.

A very instructive case in which the harmful action of quinine is fully demonstrated was referred to me by Professor Politzer, of Vienna, about two years ago.

The patient was a young lady, twenty-one years of age, an American by birth. Her family history was negative. There was no evidence of any acquired or congenital aural condition in her parents or other immediate relations. During the earlier years of her life she had the usual ailments of childhood, but never had any affection referable to her ears. She was always a robust individual and enjoyed the best of health. Six years ago she had a severe attack of grippe associated with a marked coryza. A kind neighbor, who meant well and thought he could break up her cold, gave her six five grain quinine pills, making, therefore, a dose of thirty grains. This she took within a period of fifteen minutes, the time being about ten o'clock in the evening. Two hours later she complained of an intense headache and severe tinnitus in both ears. There was no disturbance in coordination, but she noticed a marked diminution in her hearing which steadily grew worse, so that perception for all sounds was completely lost by the following morning. She did not seek medical aid immediately hoping that her lost function would in time reestablish itself. Finding that she remained deaf in both ears, she consulted different aurists with the hope that something could be done for her, and finally Professor Politzer, of Vienna, who, after a careful examination, pronounced her case hopeless.

Upon her return to this country she called upon me, and I found, upon inspection, a normal condition of the external auditory canals and tympanic membranes. There were no evidences of a previous aural trouble, and inspection of her nose and throat revealed nothing abnormal. The tuning fork tests showed an absolute loss of perception for all tones in both ears. Perception by air conduction was nil, and the vibrating fork placed against the mastoid, on either side, or on the vertex of the head, was not perceived as a tone, but interpreted merely as vibrations. In other words, there was a complete absence of perception for sounds by air and bone conduction, indicating, therefore, a bilateral, total nerve deafness. That is, we were dealing with a labyrinthine loss of hearing, in which both ears were involved.

In order to ascertain whether the vestibular portions of her labyrinths were functioning, I performed the usual rotatory tests and Bárány's test of injection of cold water

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into the external auditory canals. I noticed, after a few moments, that there was a slight nystagmus, which allowed me to assume that the vestibular part of the labyrinth was still irritable, and that the static reaction was preserved. This proved of great interest, as it clearly showed that the destruction, if caused by the toxic action of the quinine, was limited to only the cochlear portion of the labyrinth. There had been, therefore, a degeneration of the terminal filaments of the auditory nerve in the cochlear part, resulting in the complete loss of hearing, while the vestibular part had apparently escaped, inasmuch as there were no disturbances in coordination. The perception for speech was naturally also entirely lost, but through practice she acquired such a dexterity in reading the lips that one would hardly believe that she was completely deaf. Examination of the eyes did not show any changes in the fundi. About a year ago she passed through a confinement, bearing a healthy normal child. This in no way influenced her aural condition.

She received all forms of treatment, that is, injections of solutions of pilocarpine, sweat cures, electric currents, and large doses of iodides, besides local treatment of the ears in the form of catheterization, massage, etc. All these proved of no avail, so that treatment was finally abandoned.

A Wassermann test proved negative. In order to exclude the possibility of a long standing hysteria, or some other neurological condition, I had her thoroughly examined by Dr. S. P. Goodhart, the neurologist, who found no manifestations indicative of such a condition. I was therefore convinced that I was not dealing with a functional loss of hearing, but with a true organic lesion. The patient still clings to a vain hope that her lost function may be restored, and is at present receiving injections of strychnine and electric currents applied to the mastoid regions. There seems to be no change in her condition, as one would naturally expect, and I therefore have given up all ideas of restoring her lost hearing, regarding the case as one doomed to permanent deafness.

The principle upon which this form of lost hearing is based was first advanced in 1881 by Kirchner (1), who undertook a series of experiments on cats, dogs, rabbits, etc. He administered to these animals large doses of quinine, which caused paralysees of the extremities and finally death. The ears were then carefully examined, and Kirchner found hyperemia and areas of ecchymoses throughout the mucous membrane of the middle

ear and in the structures of the labyrinth. He attributed these changes to a vasomotor paralysis of the bloodvessels brought about by the toxic action of the drug. He also noticed a seromucous and hemorrhagic exudate, which, according to him, produced secondary destructive changes in the nerve endings, with subsequent loss in the hearing. Whether the changes found by Kirchner were due to the action of the drug, as he believed, is questionable, for it must be borne in mind that these animals received doses sufficient to cause death by strangulation, and this may have produced the conditions found post mortem. It has been repeatedly observed by careful investigators that hemorrhages and hyperemia of the bloodvessels have been found in the ears of animals which have been killed by strangulation alone, and not by the action of poisons.

Among these investigators was Grunert, who undertook a series of experiments on animals. He killed pigeons and mice by strangulation, and found hyperemia and hemorrhages in the mucous membrane of the middle ear and in the structures of the labyrinth similar to those observed by Kirchner. Wittmaack (2), in 1903, likewise investigated this subject and performed a series of experiments on animals by administering large and small doses of quinine. He did not agree with the explanation advanced by Kirchner, although he also found similar changes in the middle ear and labyrinth of his animals. Wittmaack did not attribute his findings to the toxic action of the drug, but was rather inclined to believe that the changes observed by him were due to strangulation and the forced respiratory acts caused by the large doses of the drug. He noticed, on the other hand, that in those animals in which the doses were small, and in which the poisonous effects were mild, these changes were entirely lacking. This would indicate that the conditions found by Wittmaack were not due to the

direct or rather specific action of the quinine, but would make one believe that they were secondary.

Wittmaack was also inclined to believe that there is an ischemia of the membranous labyrinth, similar to an ischemia of the retina, brought about by some circulatory disturbance due to the specific action of quinine. This, however, was not based on facts, as it had not been proved clinically or experimentally. Upon further investigation he changed his views. In another group of experiments on animals he found, upon more careful examinations, changes in the cells of the spiral and vestibular ganglions. That such changes take place in these ganglionic cells seems to coincide with the fact that the toxic action of quinine acts upon cells in general. It is, according to Wittmaack, a protoplasmic poison, and he therefore did not consider it surprising that it should attack the very sensitive nerve cells of one of our most sensitive organs. As the changes observed in the auditory apparatus take place so shortly after the administration of the drug, he no longer regarded them as secondary, due to circulatory disturbances, as he at first thought, but rather attributed them to a primary specific action of the poison upon the nerve cells. The primary effect of the toxic action of quinine makes itself manifest, as a rule, in the form of more or less tinnitus. This, no doubt, is brought about by an irritation of the cells of the spiral ganglion. If, on the other hand, one observes an accompanying vertigo varying in intensity, it may be assumed that there is a simultaneous involvement of the cells in the vestibular ganglion. Wittmaack therefore concluded that it was the specific action of the quinine and the circulatory disturbances, acting jointly upon the ganglion cells of the auditory nerve in the labyrinth, that most likely produced the loss of hearing in cases of quinine intoxication.

Roosa (3), who is supposed to have observed changes in the ears following the use of quinine,

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administered from ten to fifteen grains of the drug to several students. In from one to one and a half hours later he asserted to have noticed a redness of the face and auricles and a marked injection of the vessels along the handle of the malleus. He further learned that his subjects had severe ringing noises in both ears. These conditions following so shortly after the absorption of the drug in perfectly normal individuals warranted Roosa in assuming, with justice, that these changes were caused by the toxic and specific action of the quinine. Similar objective changes, however, have not been observed by other investigators.

From the foregoing, therefore, it becomes evident that we cannot regard the changes found in animals as the true cause of this form of deafness in man, and must as yet look upon this matter as an unsettled question. This is readily understood when we stop to consider that the pathological changes which give rise to this form of deafness have not as yet been clearly established, for the reason that our knowledge is based entirely upon animal experiments, and we have no record of any case in which a pathological anatomical or microscopical examination has been made of the ears of an individual who has become deaf from the toxic action of quinine. If the conditions found in animals, after the administration of doses of quinine, cannot perhaps be attributed entirely to the effect of the drug, it nevertheless seems as though it had empirically a selective or specific action on the auditory nerve. For, how are we to explain the aural symptoms and the sudden total loss of hearing in both ears in the case given above? We have here a perfectly healthy individual who completely lost her perception for all tones after taking thirty grains of the drug. She had a perfectly functioning organ of hearing prior to this, and received no other medication at the time.

That the auditory nerve is particularly sensitive to the action of quinine, as already stated, is well

known, for one often meets with individuals who complain of tinnitus and a slight impairment in hearing, even after the administration of only a few grains. It would seem, therefore, that in spite of the fact that we have no fixed data except those observed in animals to explain the phenomena, we may nevertheless regard our clinical observations as pointing to a selective or specific action of the drug on the structures in the labyrinth, and must also bear in mind that a personal idiosyncrasy plays an important part. Hence, it behooves us, in prescribing this drug, to exercise precaution, for what may seem a small or medium dose for one individual may prove harmful to another. It is extremely fortunate and also surprising that one does not meet more frequently with cases of deafness following the use of quinine, when one stops to consider the carelessness with which it is used and the quantities consumed by the laity.

Cases of quinine deafness are brought to the attention of the profession from time to time, and mention of such instances are made by Dabney (4), Tiffany (5), Shilling (6), Perron (7), and others. In all these the loss of hearing remained permanent and treatment also proved futile, as in my case.

I was prompted to report this case as I believe it is extremely interesting in that both auditory nerves became simultaneously affected, giving us a total bilateral, permanent loss of hearing. It is furthermore of interest in that the destructive changes, which apparently were due to the toxic action of the quinine, produced irreparable lesions in the cochlear portions of both labyrinths only, while the vestibular parts were evidently not involved. We can surmise this from the fact that the loss of hearing was unassociated with any disturbance of coordination. Although the cases in which the action of quinine exercises a deleterious effect upon the auditory nerve are very rare, and one does not often meet with individuals in whom this drug leaves any un-

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pleasant sequelæ, yet an unfortunate case like this ought to be a warning against its indiscriminate use.

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