

above his head a tremor commenced when it was about on a level with the shoulder, and this increased as it was raised higher, and became of wider excursion till it resembled choreic motions. In ordinary positions there was scarcely if any tremor; the arm could not be used so readily as the right. Both legs moved fairly well without tremor. Cutaneous reflex was normal; tendon reflex could not be tried satisfactorily as he could be raised only for a very short time for ophthalmoscopic examination; the change of position caused very great vertigo, and could be maintained only a minute or so. Sensation was diminished on the left. The fundus of the eyes was normal. There had been no loss of consciousness. The symptoms came on gradually.

*Autopsy.*—Dr. Cutler made the autopsy and has furnished the following notes: There was atheroma of the arteries at the base, most marked on the right of the basilar, and there it seemed to encroach upon the calibre of that artery and to interfere with some of the smaller vessels arising therefrom. On both sides at the end of the carotid there was atheroma, most on the right, and extending on that side into the middle cerebral. The right posterior cerebral was nearly occluded, but a fine stream of water could be forced through it. There were many smaller patches of atheroma dotted over the vessels of the circle of Willis.

The two hemispheres were adherent along the longitudinal fissure; this was probably inflammatory. The pia mater was moderately full of blood; no thickening except along the longitudinal fissure. On section the puncta cruenta were well marked. There was nothing abnormal in the hemispheres.

A little anterior to the middle, the pons was slightly softened; a little lower the tissue became striated, alternate yellow and gray, was somewhat translucent, resembling in color oedematous connective tissue; this mass of abnormal tissue was irregularly oval, hard to the touch, and extended with a sinuous course into the left cerebellar lobe; the left corpus dentatum was obscured by it. In the pons the new growth extended nearly to the medulla, being confined to the left side.

One sixth nerve was atrophied.

The other organs were essentially healthy.

The specimen, as I received it from Dr. Cutler, had been some time in alcohol, and I was not willing to wait long enough to see whether it would harden well in Müller's fluid. The sections for microscopic study were not so continuous and satisfactory as could be wished; but the most important parts showed well. The tumor had no clearly defined edge towards the pons, yet it could be seen that the deep nucleus of the seventh nerve was not destroyed, but just external to that nucleus the seventh nerve passed through the tumor and must have suffered in its conducting power in that part of its tract; at least that would explain the facial paralysis on the left. Anterior to the nucleus of the seventh nerve the tumor apparently approached nearer to the median line.

A large proportion of the nucleus of the left sixth nerve was healthy. In one section through the middle of the nucleus there were many degenerated nerve cells, and the number of cells was evidently less than that on the right of the same section.

The diagnosis at the time the patient was examined was tumor in the basal ganglia or cortex on the right or in the pons on the left, possibly implicating the cerebellum. The latter was considered the more probable.

Besides the conjugate deviation of the eyes the peculiar irregular motion on raising the left arm is worthy of notice. It is also of interest that there was such extensive change of the cerebellum and of part of the pons, yet no retinitis was present. The vertigo might have been expected, as it is a common symptom in cerebellar tumor. The fact that the head was drawn towards the right shoulder during the severe attacks of headache is also of interest.

The symptoms in this case are peculiar, but seemingly are easily explained. The tumor, as shown on section, did not affect the great motor tract of the pons, the pyramidal fibres which run near the anterior border of the pons, hence we have no paralysis of the right side. The facial nerve runs through the tumor, and that nerve was partially paralyzed. The tumor was situated in the left middle cerebellar crus, and extended into the pons. The specimen had been long in alcohol when I received it, and it was cut so that exactly how much of the pons was affected I could not say with certainty. Brown-Séquard has shown that lesions in this vicinity may give rise to partial paralysis on the same side with the lesion; hence the weakness of the left limbs. The spasm developed in the left arm by raising it cannot be readily explained; it was very much like the phenomenon known as post-hemiplegic chorea. The conjugate deviation was away from the side of the lesion. But in this case the regular order of symptoms was broken, for there was weakness and spasm of the left side, that on which was the tumor, and the deviation was towards the opposite side. In this regard the case is anomalous.

(To be continued.)

## THE ACTION OF QUININE UPON THE EAR.<sup>1</sup>

BY J. ORNE GREEN, M. D.

THE specific action of quinine upon the ear in producing tinnitus aurium is so well known that it is apt to be considered of no consequence, and its effects upon that most important organ, whether for good or evil, are in too many cases, it seems to me, neglected, while the attention of the physician is occupied in watching the action of the drug on the general disease for which it is administered. Many cases which have come under my observation have so thoroughly convinced me of the great injury often done by the drug, and these observations agree so well with the known pathological tendencies of the ear, and with the more recent physiological experiments on the action of quinine, that I desire to call attention to them. Works on materia medica, it is true, universally speak of the tinnitus aurium, but none with which I am acquainted seem to consider that the aural symptoms may be a contra-indication for the exhibit of the medicine in certain cases, and none give any cautions so far as the ears are concerned in regard to its use. Even so late an authority as Ringer, in his admirable Handbook of Therapeutics, contents himself by saying merely that it occasionally produces deafness, which usually passes off, but in rare cases remains for life.

Recent observations on the action of quinine show that its effect is to produce a pathological condition of the ear, which, if excessive or long continued, en-

<sup>1</sup> Read at a meeting of the Medical Improvement Society, February 26, 1883.

dangers the integrity of that organ; a pathological condition very similar to that produced in certain aural diseases, which are well known to seriously impair the functions of the ear, and that not by any occult and unknown principle, but by well-known laws of histological changes, which produce interferences with the established rules of physiology and physics.

It was formerly claimed that the action of quinine was the production of contraction of the blood-vessels, and consequently anæmia of the ear; this was early denied by Von Graefe, as contrary to his clinical experience, and any one who has watched the effects of quinine when given to a patient suffering from acute inflammation of the ear can satisfy himself in a very short time that the drug, if pushed to its specific effect, most decidedly increases the existing inflammation. I have myself watched many such cases, and consider the effect as undeniable. In 1874 Hammond<sup>1</sup> asserted that he thought the effects of the drug upon the ear were due to congestion, and in 1874 Roosa<sup>2</sup> also asserted the same thing, and gave the results of experiments performed by him upon three medical men, the result of the experiments being that the administration of the drug was followed in each case by a decided congestion of the blood-vessels, which run along the manubrium in the membrana tympani. In two of the cases there was very marked tinnitus aurium accompanying this congestion, while in the other case, that in which the congestion was the least, there was no tinnitus. The blood-vessels which were seen to be congested in these cases are known to be intimately connected with the vascular system of the middle ear; in fact, they form such an important part of this tympanic system that in the earlier stages of acute inflammation of the tympanic mucous membrane congestion of the vessels along the manubrium is one of the earliest diagnostic appearances. The blood-vessels of the tympanum are also in direct connection with the circulation within the labyrinth as has been proven by Politzer, by means of injections, and as is occasionally shown clinically by the marked tympanic congestion which accompanies inflammations of the labyrinth in cases of extension of disease from the brain to that cavity. From the very close relations of the vascular systems of these three parts, the membrana tympani, the tympanum, and the labyrinth, and from the appearance of congestion as the direct result of the administration of ten and fifteen grain doses of quinine in the carefully-conducted experiments of Roosa, we have strong evidence that the effect of the drug upon the ear is congestive rather than anæmic; but inasmuch as the amount of the congestion visible in the manubrial vessels was slight and disproportionate to the intensity of the tinnitus aurium, it seemed reasonable to conclude even from these few experiments that the congestion of the deeper cavities was greater than that seen on the periphery, so to speak, of the vascular system, and as the nervous structures within the labyrinth are the undoubted seat of subjective noises, it was probable that the labyrinth was the chief point of congestion.

Recent observations and experiments by Kirchner<sup>3</sup> confirm this view, and show that not only congestion but active inflammation and even hæmorrhage may be produced. These experiments were undertaken upon

animals with both quinine and with preparations of salicylic acid, which are well known to produce clinically the same symptoms as quinine. Two gramme doses of sodium salicylate were given to rabbits, cats, and dogs; the number of repetitions of the dose is not stated. The rabbits lived usually about a week, and died with symptoms of great dyspnoea, and with paralysis of the posterior extremities. Dissections showed great hyperæmia of the osseous meatus, near the membrana tympani, with a vesicle containing red-dish-yellow fluid, close to that membrane; the tympanic mucous membrane was dull, yellowish in color, and with numerous spots of ecchymoses, varying in size from 3 mm. to minute specks. In a number of cases opening of the labyrinth showed an intense redness on the inner surface of the stapes, and in the vestibule and the end, and perilymph was distinctly colored red. In some of the cases the ecchymoses of the tympanic mucous membrane were present only on one side, while the opposite tympanum showed enlarged and tortuous vessels.

Quinia muriate was given in doses of one to one and one half grammes. Dissections in these cases showed great congestion within the skull, the vessels of the dura and pia being very full, and of ten cases three showed with the enlarged vessels an ecchymosis in the lateral ventricle; similar conditions within the skull were also noted in cases of salicylate poisoning. With cats and dogs one to two grammes of quinia muriate were fatal in from five to eight hours, the animals showing pendulum movements of the head, increased flow of saliva, weakness or paralysis of the anterior extremities, somnolence, rapid breathing, paralysis of respiration, and death. The appearances of the ears on dissection were the same as those seen in the salicylate cases, hyperæmia and hæmorrhage of the tympanum and labyrinth. Precisely similar results were obtained from experiments on guinea-pigs and mice.

"From these observations," Kirchner says, "it is certainly evident that quinine and salicylic acid may produce changes in the important parts of the ear, which may not only injure but even wholly destroy the hearing. The involvement of the labyrinth in the hyperæmic condition could not exist for any length of time without serious injury to the ultimate nerve fibres of the acusticus. The clinical appearances of deafness produced by quinine point to the same thing; usually pain in the depth of the ear is complained of, as was also observed by Roosa, often intermittent, often very severe, and sometimes otitis externa is seen as a complication. In the examination of trustworthy persons who have declared that their deafness was due to large doses of quinine, I have repeatedly seen a marked opacity of the drum membrane, a condition which, as a rule, is to be regarded as the residuum of a chronic inflammatory process, and due to a thickening of the mucous membrane lining the inner side of the drum membrane. The symptoms in the labyrinth are also characteristic and point to an organic change in the ultimate fibres of the acusticus. Just as in syphilis so in quinine deafness we find diminution in the perception of a vibrating tuning-fork placed on the bones of the head, and a defective perception of the higher tones. In quinine deafness we are then dealing not alone with a simple irritation, a simple nervous excitation of the organ which will pass off without leaving injury, but with an inflammatory process and (possible) permanent pathological changes."

<sup>1</sup> Psychological and Medico-Legal Journal, October, 1874.

<sup>2</sup> American Journal of Medical Science, October, 1874.

<sup>3</sup> Berliner klinische Wochenschrift, No. 49, 1882.

Studies of the pathology of the ear by Toynbee (published 1841-1855), Von Troeltsch, Schwartz, Gruber, Wendt, and many others, all agree in the fact that the mucous membrane of the tympanum is especially liable to inflammation, and the changes found in that membrane, which are the causes of many forms of deafness, are histological changes of the mucous membrane, due to inflammation. The recent work by Politzer<sup>1</sup> gives more thoroughly and completely than has been done heretofore the microscopical changes which occur in the mucous membrane of the tympanum, not only in general, but in each particular part of the conducting mechanism. These observations show, in brief, that while all the structures composing the mucous membrane, epithelium, blood and lymph vessels, nerves and connective tissue, are changed in various ways in the different forms of inflammation, the connective tissue is the part in which the alterations producing permanent impairment of the functions of the conducting apparatus are most common. These changes consist in an infiltration of round cells, which becomes organized into new fibrous connective tissue by which the delicate and movable mucous membrane is converted into a hard, stiff, and adherent membrane, liable with time to a sort of cicatricial contraction, and producing immobility of the parts of the conducting apparatus covered with the affected mucous membrane. This connective tissue is subject also to still further alteration, such as calcification and ossification.

The pathology of the labyrinthine structures cannot be said to be established, the parts lie so deep, are so minute, delicate, and destructible that very few microscopists possess the ability to examine, and fewer still the inclination to devote the necessary time to, this branch of the subject. The extreme delicacy of the parts, however, and daily clinical experience in watching the effects of the common inflammations of the ear upon the nervous apparatus, as shown by the frequent loss or diminution of perception by bone conduction when there is every reason to think that the congestion from the tympanum has extended into the labyrinth, are sufficient to show us that a marked and long-continued congestion of the nervous apparatus is liable to produce serious injury.

The thickening of the mucous membrane observed by Kirchner in cases of quinine deafness is of importance as far as it goes, but too much stress should not be laid upon it, as such opacity may have resulted from some old inflammatory process, dating back even to childhood, as such are very common. It must be granted that no one yet has watched a membrana tympani normally translucent become gradually opaque as the result of quinine, but such a refinement of experimental pathology is scarcely to be expected.

The rationale of the action of quinine seems to be almost unknown. Of its effects upon the ear in producing congestion of the tympanum, labyrinth, and osseous meatus I have already spoken, and this congestion, it is fair to assume, is the cause of the well-known tinnitus aurium. Of other well recognized effects we have the frontal headache, with a sense of general fullness in the head, mental disturbance, flushing of the face, suffusion of the eyes, and, Ringer asserts, from large doses, an abolition of reflex action, before voluntary movement, due to stimulation of Setchenow's reflex inhibitory centre. In addition the last two years have developed a quinine amaurosis,

serious in its effects on the eye, and still further complicating, rather than explaining, the problem of the action of the medicine. In the *Klinische Monatsblätter für Augenheilkunde*, 1881, Knapp calls attention to sixteen cases of quinine amaurosis, which had been published or which he had himself observed. From 150 to 180 grains taken accidentally at one dose, from nine grains taken every two hours up to seventy-five or ninety grains in the course of one or two days, and from smaller doses taken for from a few days to two weeks great pallor, general weakness, twitching of the mouth and extremities, together with total blindness and deafness, came on. In some of the cases total loss of consciousness for several days existed, and the blindness and deafness were noticed first on recovery from this state. The pupils were dilated and fixed; there was not even perception of light. Ophthalmoscopic examination showed in the most pronounced cases a total absence of blood in the optic nerve and retina. In all of the cases there was a decided paleness of the papillæ, and a narrowing of the retinal vessels, both veins and arteries. The total blindness may remain for weeks or months, but in none of the cases yet observed has it been permanent. The central acuteness of vision in most of the cases returned to normal, in the remainder it varied between  $\frac{3}{8}$  and  $\frac{1}{10}$ . Light and color sense, at first much impaired, gradually became normal in the course of months. Lighter cases are reported by Knapp where, in addition to the more common general symptoms, there were clouding of the vision, diminished perception of color, and narrowing of the field of vision, with pale papillæ and contracted vessels. He has also seen the same symptoms from large doses of salicylic acid and sodium salicylate. From these observations it is evident that in the eye we have an exactly opposite condition from that as yet observed in the ear, anæmia of the retina and optic nerve instead of congestion.

From the observations on these two organs it seems evident that the effect of the drug is expended on the blood-vessels, and is probably due to action upon the vaso-motor nerve centres, although the question of the manner of this action would carry us into the realms of speculation beyond the scope of this paper.

The congestion produced in the tympanum and labyrinth fully explains the fact observed clinically that quinine may increase any existing inflammation of the tympanum. In any ear where there has been a change in the tissues such as has been described, where there is an increase in the tissue elements, and especially of the connective tissue, the result of some previous inflammation, any new congestion or inflammation produces a greater degree of deafness at the time, and is more liable to produce still further tissue changes than if the ear was in a normal state when the inflammation set in. This is due to the fact that the existing hyperplasia in the early stages of the inflammation is increased in volume by a serous infiltration, and in the later stages by an effusion of round cells which, becoming organized, add to the hyperplasia. In the acute secretory forms of tympanic inflammation any increase of the inflammation will of course add to the amount of secretion, and so intensify any previous symptoms. I have already called attention to the delicacy of the labyrinthine structures, and to the ease with which they are injured by inflammations, although the exact pathology has not been determined.

<sup>1</sup> Lehrbuch der Ohrenheilkunde, 1882.

In view of these facts and of the constantly recurring experience that patients refer their new aural symptoms or a decided and serious increase of old aural symptoms to a course of quinine, ought not the ears to be carefully considered in prescribing the drug, and especially in ordering large doses or pushing the medicine to its specific effect of tinnitus aurium? Ought not the existence of inflammation of the ears or of decided tissue changes due to previous inflammations be regarded as contra-indications to large and long-continued doses of quinine, only to be neglected in most urgent cases? It certainly seems to me that more attention should be given to its possible effect upon the ears than is often done.

Of the great value of the drug in an immense number of cases there can be no question; of its absolute necessity in many cases there is scarcely a doubt, but there still remain many instances in which, as I believe, the medicine is given in larger and more continued doses than is necessary for the slight ailments for which it is prescribed, and always with the risk to the ears. Again, there are many instances where the medicine is pushed to its specific effect from indifference or carelessness, where equally good results could be obtained by keeping within the danger line, the tinnitus aurium being the signal given by nature, at least in the majority of cases, of the congestion of the labyrinth. Finally, where large and continued doses are absolutely necessary, and where it is desirable to push the drug to its specific effect, might it not be possible to produce the desired result, and yet occasionally interrupt the administration for one, two, or three days, thus allowing the congestion of the ears to subside? Certainly a continuous congestion for a long time is more likely to result in a decided inflammation with exudation, either free or within the tissues, than an intermittent congestion.

Symptoms of acute inflammation of the ears are well known: earache, fullness, throbbing, often subjective noises, more or less deafness, etc. A few questions from the physician, even if the symptoms are not mentioned by the patient, will bring them to light. With old changes in the ears, the results of previous inflammations, the diagnosis is not so easy. The history of previous pain, severe and long continued, or an otorrhœa of some duration, even if years before, would make one suspect some tissue changes; an existing, although slight, subjective noise of any character, and any degree of deafness in either ear, would also point to the same conclusion. Certainly where any of these symptoms exist the physician should be upon his guard in prescribing quinine, and especially in giving it in large doses.

No fixed rules can be given for doses, for with this medicine, more than with many others, the idiosyncrasies of individuals to the action of the drug are most marked; while six grains in twenty-four hours produce slight tinnitus in one person, many times that amount produce no effect in another individual, and it would be interesting to know whether in the diseases in which very large doses are considered necessary, as, for instance, in severe malaria, the medicine is borne to a greater amount without tinnitus than in the same person when in a state of health.

To formulate the conclusions of this paper, we have, —

(1.) Clinical experience the world over is that quinine occasionally produces serious injury to the ears.

(2.) From our present knowledge, both clinical and

experimental, we are justified in asserting that the action of quinine upon the ears is to produce congestion of the labyrinth and tympanum, and sometimes distinct inflammation with permanent tissue changes.

(3.) That the action of the drug upon the ears should always be considered in prescribing it, and changes in the ears, due to existing or previous inflammation of those organs, constitute a contra-indication to the medicine in large doses or for a long time except under urgent circumstances.

(4.) That where large and continuous doses are absolutely necessary an occasional intermission of the administration is desirable, if possible, to diminish the risks to the ears.

## RECENT PROGRESS IN THE TREATMENT OF THORACIC DISEASES.<sup>1</sup>

BY F. I. KNIGHT, M. D.

### THE CONTAGION OF PHTHISIS.

DR. C. T. WILLIAMS read a timely paper on this subject at the last annual meeting of the British Medical Association.<sup>2</sup> He says that the discovery of the tubercle bacillus, by Koch, and the highly interesting series of experiments which led up to it, have naturally caused us to review phthisis in its various aspects, and especially in that which relates to contagion. How far consumption is infectious is a question which has been under discussion for centuries, and on which great difference of opinion has prevailed, and still prevails, in various countries, the north of Europe holding, as a rule, its non-contagiousness, and the south its contagiousness. The chief difficulty lies in the fact that many of the most potent agents of causation in phthisis, such as dampness of soil, bad ventilation, and deficient food, are also conditions which would promote the multiplication of low organisms; and, on the other hand, heredity, which is the source of a large amount of phthisis, cannot be reconciled in its action with the bacillus theory; for, if a man had strongly inherited phthisis in his tissues, are we to believe the bacilli have been transmitted in the seminal fluid of his father? How can we account for the cases where the parents having died of consumption the children are necessarily attacked, on arriving at a certain age, with a severe type of the disease? [This does not seem to us necessarily an argument against infection. The child may inherit not the germ, but such a condition as makes him, at a certain age, more liable than others to infection, that is, he offers a more favorable soil for the development of the germ. REF.]

The microscope tells us that Koch's bacilli are present in phthisical sputum in fair abundance. Now, when we consider the number of consumptive people who, being under no restriction, go about coughing and expectorating freely in the streets and parks of London, and remember that this sputa abounds in bacilli, that it dries, and becoming dust is wafted about in the atmosphere, and doubtless inhaled by a large proportion of the population, we must admit that the bacilli, though ever present, are not very active in ill doing, and probably because the soil they enter is not always suitable.

The forms of contagion in phthisis which have been most discussed are the following: (1.) Infection

<sup>1</sup> Continued from page 197.

<sup>2</sup> British Medical Journal, September 30, 1882.