SOME ANALOGIES WHICH FAVOUR PROTOZOAL HYPOTHESES OF BERI-BERI.

BY C. M. HEANLEY, M.B., D.P.H., D.T.M.,

Assistant Medical Officer, Plaistow Fever Hospital.

(Late Plague Medical Officer, Punjab Government.)

IT has long since been remarked that beri-beri in its etiology shows resemblances to malaria and yellow fever. Of recent years a number of diseases, notable features of which are that they are strictly limited to places having a warm temperature and that they show groups of obviously related cases though the patient *per se* is not sufficient to convey infection, have been shown to be due to protozoa. Malaria, kala-azar, probably yellow fever and possibly sleeping sickness are to be reckoned amongst them. In fact so many diseases which display the above characters have been shown to be caused by protozoa that the occurrence together of these features may be said to establish a considerable probability that a disease if infective is caused by an organism which has a more complicated life history than a bacterium. The great majority of diseases due to known bacteria are obviously at times directly contagious; of the exceptions cerebro-spinal fever and tetanus are about the only ones which can be said to show place infection and grouping of cases in any way comparable with what is seen in beri-beri. Thus the limitation of this disease to places having a warm temperature and the harmlessness of the patient apart from his surroundings would, if the disease is due to infective organisms, tend to place it by analogy amongst protozoal rather than bacterial diseases.

Again it seems at first thought unlikely that any human disease, in the spreading of which direct contagion appears to be an important factor, would be confined to places having a warm temperature. For how can the germ be disadvantagiously affected during direct transference? Nevertheless such diseases do exist, and if we enumerate them—tinea imbricata, pinta, pemphigus contagiosus, yaws, verruga peruviana, dengue, yellow fever and possibly a few others such as ulcerating granuloma—we find that they are, with the exception of yellow fever and dengue, either simple skin lesions in which the germ must be exposed to the climate or diseases in which the output of material is through extensive lesions of the skin. Of the exceptions yellow fever has been shown to possess a false appearance of direct infection. The fact that dengue now stands alone establishes a probability that it also presents a false appearance of direct infection. Work has been done which tends to show this (Graham, *New York Medical Record*, February 8th, 1902). Although bacteriology does not enable us to define a group it would be equally unlikely that a bacterial disease other than a skin lesion, in which passive persistence apart from growth of the germ outside the body was a factor in spreading the disease, could be rigidly confined to places having a warm temperature: for the effect of cold is rather to preserve than to destroy bacterial organisms. If beri-beri were directly infectious or if infection could be due to passive persistence, as opposed to growth, of infective bacteria deposited in the surroundings of the future host, then it is very unlikely that it would be rigidly confined to places having a warm temperature. It is therefore reasonable to suppose that beri-beri is confined to such places either because a germ, infective or otherwise, is obliged to grow outside the body and requires a warm temperature in which to do so, or because it is caused by an organism which needs a special agent to transmit it or which must undergo further development along a life cycle before it again enters man. The multiplication of infective bacterial germs outside the body in natural conditions is difficult to prove. Though it is almost certainly necessary for the continued propagation of some diseases, in extremely few that are due to known bacterias can it be such an important factor and so dependent on heat that the disease is obliged to remain permanently in places having a temperature as high as that required by beri-beri. Malta fever and mycetoma may approach to being exceptions. Cholera and bacterial dysenteries though sometimes called tropical show extensions far into temperate zones. The theory that beri-beri is due to growth outside the body of an organism, the toxin of which is absorbed, has few or no analogies except amongst diseases traceable to the ingestion of special foods. Moreover, it would explain very well a large number of observations on tropical protozoal diseases especially the group bearing on the harmlessness of the patient apart from his surroundings; we made the word malaria and found a protozoan. The theory does, however, stand alone in the readiness with which it explains the early improvement of the patient when removed from infected place.

The supposition that beri-beri is confined to places having a warm temperature because the organism may be transmitted by a special insect or because it must go through further stages of development in a life cycle more complex than that possessed by bacteria before it can again infect man finds many analogies among tropical protozoal diseases.

Beri-beri shows many close analogies to malaria. It resembles this disease in being favoured by heat and damp, in being a place infection and attacking those who sleep near the ground. The outbreak of beri-beri in the individual is like malaria apparently as dependent on physiological depression and other factors as on an incubation period with definable limits. Beri-beri like malaria if nursed in hospital in cold climates never spreads to other patients or to nurses. Hospitals within the endemic area may become infected but rarely do so, though scores

of patients may be aggregated. In places where there is a hot and cold season, such as Japan, beri-beri, like malaria, crops up at the beginning of the warm season, continues and gradually increases throughout the summer and dies out almost entirely as far as fresh cases are concerned in the winter. In the tropics it occurs all the year round but is generally more prevalent in the rainy season. As in case of malaria the mortality is generally greatest in low latitudes. Beri-beri resembles malaria in its chronicity, in its tendency to relapse and recur it may be annually in the subject, in perhaps the ultimate acclimatisation which is said to occur, and in the lesser susceptability of those residing permanently in endemic areas. Beri-beri resembles malaria in being a house disease. It is also an institutional and gang disease (H. E. Durham and others). Sambon has pointed out an instance in which it was markedly a gang disease but failed to be a house disease (*B. M. J.*, Sept. 1902). Now the distribution of infected anopheles has shown malaria to be to a considerable degree a house disease. It is also a gang disease, for it has, I think, been conclusively shown that the virulent malaria which breaks out on extensive disturbance of the soil is due to the collecting together of men, and the crowding of susceptible persons, good crescent cases and anopheles mosquitoes under the same roof. Malaria attacks the sexes nearly equally and is a disease of all ages but especially of childhood; beri-beri, though a house disease, is far less often seen in women, children and the aged than in working men who spend less time indoors. The explanation of the curious age and sex incidence of beri-beri is probably to be found in the fact that it is a gang disease.

When we think of the way diseases counterfeit each other and digress from type we shall scarcely look upon similarities in signs and symptoms as an indication of a similar cause, but it is natural to ask whether the features of beri-beri show any marked resemblance to those of diseases due to protozoa. The œdema of beri-beri is firmer than that of nephritis and may occur in transient patches; it is not unfrequently general. The occurrence of firm general œdema and firm patchy œdema is somewhat rare in disease, but is a marked characteristic of the protozoal disease trypanosomiasis. In this connection may be mentioned the facies of both diseases. In protozoal affections we might look for a large mononeuclear leucocytosis and marked enlargement of the spleen, but these are not found in yellow fever.

Beri-beri, in regard to its etiology, has been shown to present many close analogies to malaria. If this is due to its cause being highly specialised on similar lines, then the points which do not compare will indicate ways in which the causes differ. It would appear that all the factors necessary for the contraction of beri-beri may be found existing within the limits of a hot and dirty dwelling in a climate otherwise unfavourable. This is not so in malaria; moreover malaria is a rural disease; beri-beri, more a disease of towns. These differences could be explained by assuming a different intermediate host or the absence of one in beri-beri.

In trying to form details of a protozoal hypothesis of beri-beri which shall roughly resemble that of malaria we have to consider the much emphasised point that in bad epidemics the patient will probably show improvement in two or three days if he can be removed, but not if he is left in the infected place. A conceivable explanation of this might be found in a frequent introduction of the germ and a rapid subsidence of its chief toxin producing phase: we should not expect this phase to go on actively for many days as in malaria without re-introduction or a period of latency. A latent form would, as in malaria, account for elements in relapse and chronicity. And a comparatively non-toxic long lived form, perhaps the same as the latent form, perhaps a gamete as in malaria, would account for the obscure origin and long latency of outbreaks and the fact that beri-beri is a disease of assembled men. Consider a person in a highly malarious region who is beginning to show serious symptoms the result of chronic malaria. If he is left he will probably get worse, removal will probably lead to his recovery. If we could raise the endemic index and shorten the acute disease resulting from a single infection, the result would approximate to that observed when a person sufferiug from beri-beri is left or removed from the place where he has contracted the disease.

In looking for a hypothetical intermediate host we shall expect that it is to be found, (1) in towns, (2) in occupied dwellings, (3) in inhabited parts of ships that have proceeded long since from warm to cold climates, and (4) we should expect that it is not sufficiently self motile, at any rate when infected, to move from one house to another or readily even from room to room.

Conditions 1 and 3 would exclude many mosquitoes; they would not, I think, exclude stegomyia fasciata; 4 probably would exclude it. None of the above restrictions would exclude fleas, bedbugs or pediculi. The thermal limitations of beri-beri might be thought to weigh against the probability of pediculi, or to necessitate ovum or larva infection in the case of fleas. An intermediate host has been assumed for the sake of closer analogy; there is no absolute necessity for it, though the difficulty of disinfection would tend to indicate one. In its absence we might suppose that a protozoan germ after leaving the body is obliged to develop further in warm moist places before it can again enter man through skin, sores, or other surfaces. Theories of disease must present a reasonable explanation of the facts which have been observed with certainty. They also as a rule follow naturally

upon what is known of other diseases, indeed, their rationality is intimately bound up with this; for instance, Hamilton Wright's theory follows naturally upon diphtheria and other diseases. It may, I think, be claimed that in the above respects protozoal theories of beri-beri have, by recent discoveries in tropical pathology, been raised to a level of probability scarcely inferior to the theories of Manson and Hamilton Wright, that they serve to keep in mind the necessity of examining the fresh tissues and the fluid in the œdematous patches by the most recent methods, and that they urge the useful search for and study of protozoal parasites in insects found in association with man. In some trypanosoma infections the organisms are found with extreme difficulty except in the œdematous patches. Although the parasite of beri-beri may be ultramicroscopic or otherwise undemonstrable in man, we know that in malaria and we believe in yellow fever that the organism is far larger in the alternate life cycle.

A Mirror of Hospital Practice.

ORBITAL SARCOMA—KRONLEIN'S OPERATION.

BY C. P. LUKIS, M.D., F.R.C.S.,
LIEUT.-COLONEL, I.M.S.
(*Late Civil Surgeon, Agra*),
Principal, Medical College, Calcutta.

LACHIA, Chamar, aged 45 years, was admitted into the Ophthalmic Hospital, Agra, on February 28th, 1905, giving the following history:—

About six months ago, one day, while chopping bundles of hay, a heavy chip struck his left eye. Since then the sight in that eye has gradually failed, and he has noticed steadily increasing protrusion of the globe; but at no time since the injury has there been any manifestation of inflammatory symptoms or pain of an acute nature. He has merely complained of a sense of heaviness and tension. It is possible, therefore, that the accident was merely a coincidence, and has no causal significance.

The following note describes the condition at the time of admission. There is a swelling under the left upper lid pushing the eyeball bodily downwards, outwards and forwards, causing considerable proptosis. Theeyeball has thus come to rest almost on the malar prominence. On raising the eyelid a distinct tumour can be seen wedged in between the eyeball and the roof of the orbit; it appears to be larger than a walnut, rounded in shape, and elastic to the touch. It is slightly moveable, and distended vessels can be seen crossing its surface. There is considerable lacrimation, the cornea is clear, the anterior chamber shallow, and the pupils moderately dilated and fixed, other media clear. On ophthalmoscopic examination, a uniform greyish haze appears all over the fundus, the disc can be made out with difficulty, its surface being blurred and hazy, and the outline indistinct. The patient is stone blind and has absolutely no perception of light in that eye. General health fair.

Operation.—Assistant-Surgeon C. M. De, in charge of the Ophthalmic Hospital, having brought to my notice Dr. F. P. Maynard's account of a successful operation performed by Kronlein's method (*Ophthalmic Review*, June 1904), I decided to perform a similar operation in this case. Accordingly on the 3rd of March, the patient being anæsthetised, and the left temple and eyebrow having been shaved and rendered aseptic in the usual manner, a curved incision, with the convexity towards the outer canthus, was made down to the bone, extending from the temporal ridge to the zygoma. The flap being turned backwards, the periosteum on the outer wall of the orbit together with the lachrymal gland was then raised and pushed towards the eyeball, and kept away with a retractor during the rest of the operation. The periosteum over the external angular process of the frontal bone was next raised, and then gently separated with an elevator from the bone over the whole of the external wall of the orbit. The external angular process was then grooved with a Heys' saw about half an inch above the fronto-malar suture, and finally cut through with a chisel. The chiselling was next continued obliquely backwards and downwards through the great wing of the sphenoid to the spheno-maxillary suture. Lastly, the frontal process of the malar bone was sawn through horizontally, and the piece of bone thus marked out was turned outwards. The chisel not being a very fine one, the small piece of bone above the fronto-malar suture here became separated and was removed.

The orbital periosteum was then slit up from before backwards, and the tumour being now exposed, was shelled out with the finger. This was accomplished without any difficulty and it was not necessary to cut any of the ocular muscles. The bone was then replaced and the skin brought into position with horse-hair sutures; a horse-hair drain being left in the outer angle of the wound. The eyeball now completely receded into the orbit, and the lids were closed over it.

Two points need to be particularly noted about the operation:—

1. By not slitting the external canthus, as was done by Dr. F. P. Maynard in his case, the conjunctival sac was preserved intact, and there was therefore no risk of bacterial infection of the wound.

2. No division of the ocular muscles was made, and therefore there was no danger of deviation of the ocular axis after repair.