Periodicity in the Daily Numbers of Filarial Embryos at the same Hour of the Evening.

The periodical variations in the number of embryo filaria in the peripheral blood at different hours of the day and night is well known, but as far as I am aware less attention has been paid to the variations at the same hour from day to day, such as are well illustrated in the latter part of the upper curve of the four cases in which the antimony treatment failed permanently to reduce their numbers. During the four months from October to January there was a regular rise in the numbers at about new moon, and a fall at full moon, which is very suggestive in view of the popular opinion that filarial fever is influenced by the phases of the moon. To examine this hypothesis further I have plotted out the curves of each of the four cases separately, and found that in two months three of the four curves followed this rule, but in the other two months only two of them did so, which indicates that the coincidence in the combined curve is probably accidental. Moreover, the daily counts in the control cases showed great fluctuations occurring at shorter intervals and less regularly. These daily variations are deserving of more detailed study, as they may well furnish a clue to the periodicity of filarial fever, which has always puzzled me, but which may possibly be explained, if the fluctuations referred to are produced by a periodical discharge into the circulation of a large number of newly-born embryo filaria, as, indeed, has been suggested by Bahr. As long as the lymphatic channels are free this need not cause any material inconvenience to the host, but when the lymphatics become blocked by inflammatory changes, then such a brood of young embryos may well cause some further blocking of the lymphatic channels with the excitation of inflammatory changes in the already damaged tissues, without invoking the aid of Manson's hypothesis of the abortion of immature ova. Secondary infections, with staphylococci and streptococci, doubtless also often play an important part in the febrile process, as I (unpublished records), as well as others, have cultivated these organisms from the inflamed superficial tissues of the legs in cases of elephantiasis and obtained considerable amelioration of the febrile attacks by auto-vaccines. On the other hand, cultures during these attacks have often failed, while the frequently very regular periodicity in filarial fever attacks could be more easily explained by the above hypothesis, which may serve a useful purpose if it stimulates further research into the variations of the filarial embryos in the blood from day to day on similar lines to those adopted in my present research, which circumstances will not allow of my continuing at present.

Further Investigations at Puri by Dr. P. N. Das.

In my first paper I mentioned that Dr. P. N. Das was continuing the investigation I commenced at Puri with his help, and he has kindly sent me reports of his progress. As he recently read a paper on the subject at the Indian Science Congress at Nagpur, which will eventually appear in the *Indian Journal of Medical Research*, it will suffice here to say that in five out of eight cases the embryo filaria had completely disappeared from the peripheral blood after from twelve to thirty-seven intravenous injections of sodium antimonyl tartrate, and had remained absent for from a few days up to one month and a half, while in the remaining three cases the parasites had become greatly reduced. Moreover, in two additional patients, who were suffering from weekly attacks of filarial fever, the attacks had ceased under the treatment, and in one case had remained absent up to three and a half months. These are most promising results.

Recent Cases Treated by the Writer.

The following brief notes of cases recently treated by me may also be of interest, although I cannot follow them up very long, as I am about to proceed on leave.

CASE I.—Early Elephantiasis.

A European lady consulted me for recently developed swelling of the forearms just above the wrists and of the feet highly suggestive of commencing elephantiasis. The evening blood showed 50 embryo filaria in 20 c.mm., so I gave thirteen injections of sodium antimonyl tartrate, mostly in 4 c.cm. doses, into a small wrist vein, which was the only one available. At the end of this course the swelling had gone down by nearly an inch, only two filaria could be found in 20 c.mm. of blood, and she had lost the slight periodical febrile attacks she formerly suffered from.

CASE II.—Filarial Orchitis.

A European patient was admitted to the General Hospital for orchitis; numerous filaria were found in his night blood. Major Green Armitage, I.M.S., very kindly treated him with sodium antimonyl tartrate, and sent me blood films of measured quantities taken at 10 p.m. Counts on five consecutive evenings prior to treatment varied between 44 and 96, and averaged 64. They were also made on alternate evenings while the injections were being given daily, working up to 4 c.cm. of the 2 per cent. solution. During the first ten days of the treatment the filaria varied between 21 (the first day) and 5, and averaged 9, while the next three counts gave 4 on one day and none on the other two days. Another count after only one injection had been given in four days also showed only one embryo in two slides, so as the decrease of the drug has not been followed by any definite increase in the filarial embryos the result is promising.

CASE III.—Chyluria.

I am indebted to my colleague, Lieut.-Colonel D. McCay, I.M.S., for an opportunity of treating this Indian patient in the Medical College Hospital. The average of four counts before treatment showed 86 embryo filaria in 20 c.mm. evening blood. The man then received nine injections of a 1 in 500 solution of colloid antimony sulphide, varying from 2 to 6 c.cm., such as I have previously found to be more effective in kala-azar than sodium antimonyl tartrate, while it is very much less toxic for man. This solution, however, failed to reduce the filarial embryos, which averaged 93 on the evenings of the injections. As the solution employed contains only approximately one-fifth the amount of antimony in the sodium tartrate this is not altogether surprising, as such a worm as the adult *Wuchereria bancrofti* is likely to be more resistant than a minute protozoal parasite to the prolonged action of a colloid preparation, which is retained in the blood longer than a soluble salt.

Dr. P. N. Das has just reported to me four cases in which 5 to 6 injections up to 5 c.cm. doses of the colloid preparation also failed to reduce the filarial embryos, so it is evidently not very active against them, although longer trials might possibly yield better results.

CONCLUSION.

The results above recorded appear to indicate that intravenous injections of soluble antimony salts have a definite effect in greatly reducing or causing the disappearance of the filarial embryos from the peripheral blood, presumably as a result of the destruction of the adult filaria, as the effect may last in some cases in an increasing degree for several months after cessation of the treatment. Moreover, clinically favourable results have been obtained in a few cases of filarial fever and elephantiasis. A rather long course of intravenous injections of a highly toxic drug is, however, required to produce this effect, so the new method of treatment requires care in its use, and much further experience will be necessary before its precise value can be decided.

CYCLOPLEGIA IN ROUTINE REFRACTION WORK.*

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ONE of your number recently put a question to me which may very well form the subject of our consideration to-day. He asked: "What is the best means of obtaining cycloplegia for routine refraction work in children?" That is a very pertinent question. There is a vast amount of refraction work being done for children. A cycloplegic is necessary for satisfactory work. We must be satisfied of the efficiency and safety of the drug used, and that the manner of its usage gives the least inconvenience to the child, its parents, the school teachers, and to your own department where the eye work is done. It is scarcely necessary to defend the statement that cycloplegia is necessary for satisfactory work in children. It is true that, given unlimited time, much skill in handling children and in the use of the mirror, it is often possible to make a good retinoscopy without a cycloplegic; but the most experienced will agree that, even under the best conditions, the results so obtained are open to doubt. When, however, we have to deal with a dozen or more children at the out-patient department of a hospital or a school clinic, it is manifest that without a cycloplegic the work could not be done at all.

* A lecture delivered at the West London Post-Graduate College.

The choice of drugs is happily limited. Homatropine and atropine are the only effective claimants for attention. Hyoscyamus was extensively tried a few years ago, but some rather startling experiences of its toxic effects damped the enthusiasm of its most ardent advocates. I would counsel you to leave this drug severely alone for diagnostic purposes. Homatropine and atropine have each strong points in their favour and it will be well to weigh these.

Homatropine.

Homatropine is a most valuable drug. It is quick in action. Its effects pass off speedily and they can be neutralized at will. I have never known it produce toxic symptoms when administered in the way set out here. Its disadvantages are its high cost and the care necessary to get efficient results. We may use it in a watery solution of the salt, the oily solution of the pure alkaloid, or in one of the minute solid discs or tablets prepared by well known firms. The cost of the drug should rule out the use of the watery solution, at any rate in hospital practice. There is a story that a well known manufacturer of mustard said that he made his fortune out of the mustard that folk left on their plates. Priceless quantities of homatropine have run down the cheeks of patients and watered the floors of out-patient departments. Further, to secure full effects, two to four instillations are required, spread out over an hour. These disadvantages can be overcome by thickening the watery solution. I did this during the war when the pure alkaloid necessary for the preparation of the oily solution was scarce. To the watery solution of the salt small lumps of gum arabic were added and allowed to dissolve until the solution was so viscid that it could be lifted in drops with a narrow probe. If this gummy solution be used it must be made antiseptic, otherwise moulds speedily grow in it. I have found the addition of menthol gr. 2, ol. gaultheria minims 2, and tincture of iodine minims 2 to the pint of water makes a most efficient preservative both for this gummy solution and also for watery solutions of cocaine.

The oily solution of the pure alkaloids of homatropine and cocaine, 2 per cent. of each dissolved in castor oil, forms, in my experience, the most convenient and efficient quick-acting cycloplegic. It needs very careful preparation. The mixture must be warmed gently over a water bath for some six hours to secure solution. Too high a temperature will cause some of the homatropine to be reconverted into atropine, so that the brevity of the effect of the homatropine is lost. The advantages of the oil lie in the small quantity needed and the single instillation. One drop, no larger than the head of a wax vesta, will secure complete cycloplegia of the eyes of a child within one hour, provided it be properly used.

Some years ago, in furtherance of a piece of research work, I worked out the refraction of all the children in a large higher grade school; 1,100 children between the ages of 4 and 14 years were examined. The method adopted was as follows:

Three rooms were chosen leading from one to the other. The group of children to be examined were collected in one with a teacher; one by one they came into the middle room where their eyes were anointed; then each passed into the third room where it was put into a seat and told to put its arms on the desk, its head on its arms, and go to sleep. There they remained for a full hour, when they were told to sit up and look about until wanted for examination. After the examination the effect of the drug was neutralized by the instillation of a minute droplet of eserine 1 per cent. in castor oil, so that the pupils of the eyes were closed down before the children left school. The examination was made with the consent of the parents, many of whom were present at the time. Certain euphemisms helped a successful working. The first instillation was described as "smoothing the eyes with oil," the second as "washing out the oil." That satisfied parental desire to know what was being done. At the first instillation the child was told that it would "tickle"; that made the smart of the oil (rather like soap getting into the eyes) seem a joke. If the smart proved too much for some child so that it cried the fact that no other children were present prevented the disturbance affecting the rest of the children.

The actual instillation of the oil needs skill. The oil should be lifted on a short probe no thicker than a wax vesta. Large glass rods lift too much and make a mess. The child should be told to look at the surgeon's eyes. The surgeon with thumb and forefinger of left hand pulls down simultaneously both lower eyelids so as to expose the conjunctiva, then quickly first one then the other lid is touched with the same oil drop before the child has time to blink. If a blink intervenes between the two anointings the smart will cause the child to screw up its lids, so that the second anointing may be impossible or a failure.

Once the oil is on the conjunctiva it spreads over the whole area; it cannot be rubbed out or washed out by tears. It is absorbed over a large area simultaneously and is consequently most effective. The hour of quiescence of the child prevents the muscles striving against the action of the drug. I adopted this practice after noting how quickly deaf children reacted who, after anointing, were kept in a darkened room; with a total absence of stimuli most of the children fell asleep, and cycloplegia was obtained exceptionally quickly. A last point remains to be noted. The children are told to open the eyes and look about shortly before the time of the examination. This is to secure by blinking that the remains of the oil shall be swept away and the cornea left clean and bright.

If some of the eyes be examined by the plane mirror reflex before the completion of the cycloplegia, a curious phenomenon may be noted. The reflex seen in the full round pupil may be divided into two zones separated from each other by a bright circular line, just as though the nucleus of the lens had a different refractive index to the outer layers of the lens. I take it that this is an indication of the gradual relaxation of the lens fibres as the influence of the ciliary muscle is withdrawn, for I noted the phenomenon most often where the error of refraction was a considerable degree of hypermetropia. If at the end of the hour a child's reflex should show this ring mark, the child should be put back to wait a while longer.

With such a procedure as the foregoing, the oily homatropine and cocaine solution can be most efficient and safe in routine refraction work. But it will be evident its use requires time, patience, and spacious premises. A crowded out-patient department does not furnish these conditions, the risk of one child of uncertain temper upsetting the rest of the children by an outburst of crying is great, so that for routine hospital work I prefer atropine for home use.

A word must be said on the solid preparation of homatropine. The minute tablets or discs are most convenient for travelling purposes; they are clean, dry, small in bulk, and efficient. But they are niggly little things, and for that one reason I do not find them so satisfactory for routine use as solutions.

Atropine.

Atropine requires several hours to attain its full action. Once its action is established it is a week before it passes off, and it cannot be neutralized by eserine. Its slowness of action makes its instillation at the same session as the main examination impossible; so that after the child is seen at the first session, atropine must be ordered for home use until the time of the next examination. The loss of accommodation for a week to ten days is unpleasant to children of older years, and their work in the school is practically stopped for the time. These are the real drawbacks of its use; but they are small when balanced by the convenience which its use presents in the heavy routine work of an eye department.

Atropine may be prepared in four forms—(1) watery solution, (2) oily solution, (3) tablets, (4) ointment. The watery solution I rule out because of its extravagance, so much of a watery solution is wasted. Further, bottles and droppers are required and these are costly. The oily solution is also ruled out, for the more costly alkaloid is needed and also bottles. The tablets should, in my judgement, be ruled out also, for the average patient of the hospital class is not up to the task of placing these minute discs within the eyelid. The tiny disc has to be shaken out of a glass tube, picked up with a brush or rod damped to make it adhesive, then the disc has to be transferred to the eyelid. Parents will damp brush or rod by putting it to their lips, an unwholesome procedure. Discs get lost. There is a risk that small children may think they are sweets. And, finally, there is the risk that parents may use pointed instruments to insert the discs and possibly damage the eye of the child by a sudden jerk of the hand or of the child's head.

The use of the ointment avoids these difficulties, and presents certain advantages. It can be kept in bulk in the dispensary, put up in small cardboard boxes ready labelled with a red "poison" label in the quiet times of the dispensary officers, and served out rapidly when the rush comes. I had the curiosity recently to examine the supply issued by the Belgrave Hospital Dispensary. The boxes contained sufficient for use thrice daily for one week. Several specimens were weighed up, and it was found that the average quantity weighed nine grains, the extremes were 7 and 10 grains. The dispenser therefore showed

good judgement in picking up the required quantity with the knife-point.

At the Belgrave Hospital printed directions for the use of the ointment are given to each parent by the surgeon in charge. They read as follows:

BELGRAVE HOSPITAL FOR CHILDREN.
Eye Department.

Put a small piece of the ointment (the size of a match head) inside the lower lid of EACH eye three times every day, after breakfast, dinner, and tea, until you come next time. Use a wax match with the head cut off to put in the ointment.

The eyes will open wide, and the child will not be able to read, but may go to school. The ointment will be stopped when the doctor has examined the eyes and ordered the glasses.

Do not forget to use the ointment, or your visit will be wasted. Be careful with it, for it is very costly. Do not let any one else use it.

From an experience of many years I find these directions are readily understood and carried out by the parents. They have a further advantage, in that the simple explanation of the reasons for the use of the ointment, its effects, and their duration forestall objections from querulous parents.

On the second visit a nurse looks at each child, and should she find one in which the effects look incomplete, she at once puts a drop of the oily homatropine into the eye; the child is put to the end of the row, and is ready for examination when its turn comes.

There are some children for whom this routine practice is unsatisfactory. Children with chronic blepharitis or eyes scarred from relapsing phlyctenular ulcers often react badly to atropine. These are directed to attend very early at the next session, when the nurse prepares them for examination by instilling the oily homatropine.

Adults.

It may be convenient to end this lecture by making a few observations on the use of these drugs for adults. For the examination of young adults, let us say for those over school age up to 30 years, a cycloplegic is often necessary. It should be a rule never to use atropine for these for purely diagnostic purposes. The discomfort and loss of effective work occasioned by the suppression of accommodation and pupil reaction for a week or more is serious, and should be avoided. Consider the circumstances of a clerk, of a seamstress, or of any other skilled worker whose near vision is put out of action in this fashion, or of a driver whose eyes are dazzled by the blaze of light entering his widely opened pupils. In all but the rarest cases the oily homatropine and cocaine solution will do the necessary work then and there, and its effects can be neutralized speedily by a final instillation of the oily eserine. Cases of suspected spasm of the accommodation are few and far between; in these atropine is needed, and should be ordered for home use with due explanation.

In adults over 30 years of age atropine is never needed for diagnostic purposes. It is not only a serious inconvenience to the patient by reason of the dazzling and disturbance of near vision, but there is a serious risk of glaucoma in susceptible subjects. For these reasons, where a mydriatic is needed for effective examination—and you will note that I here use the term “mydriatic” and not “cycloplegic”—the mydriatic should be homatropine. As little as is possible should be used, and that little should be neutralized by eserine before the patient is allowed to leave the consulting room.

THE TREATMENT OF MALARIA.

BY

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The methods advocated for the treatment of malaria are innumerable. After experience of many hundreds of cases of malaria amongst Europeans in the campaign in East Africa, and after suffering severely myself from repeated attacks, I came to certain definite conclusions as to the treatment of this disease.

1. Routine “stock” treatment often fails, and is justifiable only when the medical staff is insufficient to deal with the number of patients. Every case has its peculiarities.

2. Antimony plays no part in the treatment. Arsenic is most useful in the convalescent stage, especially in

cachectic cases, and after the acute stage of blackwater fever, when one or two intramuscular injections of “914” have often seemed to be beneficial.

3. After a preliminary dose of calomel or blue pill, quinine, preferably the hydrochloride, should be given as early as possible in an attack of malaria. *Bis dat qui cito dat.* Ten grains in a small quantity of water should be given every three hours to a maximum of 45 grains. The aim should be to produce tinnitus aurium, and the dose regulated accordingly. The heroic dose (20 or 30 grains) is not more effectual than the smaller, and is far more liable to incite vomiting. I doubt whether, by the mouth, one can absorb more than 10 grains of quinine during the course of two or three hours. At the same time the patient should drink freely of water, lemonade, etc. But all food, even milk, should be withheld during the acute stage, and even for several hours after defervescence.

4. In most cases this form of treatment will suffice. Vomiting is the commonest and most troublesome complication. A dose of quinine, if rejected, should be repeated—two or three times, if necessary. A little firmness is often necessary, especially with a patient who has made up his mind that he cannot retain quinine. A large tender spleen, which often incites vomiting, is less felt after the application of a plaster and by lying on the left side.

5. The chronic cases present the greatest difficulty. We rely too much on drugs and pay too little attention to the stimulation of the patient's natural powers of resistance. The advocates of various forms of treatment in claiming their successes forget the *vis medicatrix naturae*. Even quinine fails when a patient is kept in a relaxing, unhealthy climate; while in healthier surroundings relapsing cases tend to get better, even without the use of drugs. I do not believe in the long-continued administration of quinine, even in small doses, whether as a curative or as a prophylactic measure. I suspect that the *plasmodium* becomes resistant to quinine in course of time; or perhaps the drug, owing to its irritant action, becomes less easily absorbed in the intestinal tract.

In chronic cases the relapses should be treated intensively and early. To give quinine between the attacks is to bombard the enemy's line when he is safe in his dug-outs. Rather the aim should be to catch him when he makes his raids.

6. Only in cases of uncontrollable vomiting, in cerebral and in a few other complications will it be necessary to administer quinine otherwise than by the mouth. In my opinion, subcutaneous and intramuscular injections are always contraindicated. High rectal and intravenous injections, slowly given, rarely fail to influence an attack in the acute stages. The most useful proof that we have of the absorption of quinine is the production of tinnitus aurium and slight deafness. Only after big doses and a long interval (a day or so) did we obtain this effect after subcutaneous and intramuscular injections. There is no evidence that quinine is absorbed sufficiently quickly from the muscles and subcutaneous tissues to be of any use in an attack of malaria, and the other disadvantages are obvious.

7. A great physician said that a man who could not control malaria with quinine should give up the practice of medicine. Drugs must be given with the head as well as with the hand. The ideal of a *therapia magna sterilisans* has so far proved illusory. Quinine is as much a specific in malaria as is arsenic in syphilis, but in both cases there is a time to give and a time to refrain from giving.

8. Blood films should be taken not once but several times during the course of an attack, and treatment judged and regulated accordingly.

Attention to these details will, I think, be rewarded by greater success in the use of quinine by the mouth than seems to be the experience of many medical officers, and more complicated methods of treatment will more rarely be necessary.

The following extract from Buchan's *Prevention and Cure of Diseases* (London, 1774) is of interest:

After proper evacuations, the patient may safely use the Peruvian bark. Two ounces of the best jesuit's bark, finely powdered, may be divided into twenty-four doses. In an ague which returns each day one of the above doses may be taken every two hours . . . in a tertian, or third-day ague, it will be sufficient to take a dose every third hour.

There is much other sound advice, and the last words of the chapter on agues are “the only method to obtain a