doses, but now very seldom employ less than half a grain at a time, and often give as much as two-thirds, the equivalent of 60 grains of ipecacuanha, and have twice injected 1-grain doses subcutaneously without any vomiting or depression, but such a quantity is only required in extremely acute amoebic dysentery. The salts can be safely boiled for a very short time, but it is better to dissolve them in sterile saline, or to boil the solution first and then add the emetine salt. I have arranged with Messrs. Burroughs and Wellcome to put up the drugs, both as tablets and already dissolved in sealed ampoules, while Messrs. Parke, Davis are also supplying them in the latter form.

The Value of Emetine Treatment in the Differential Diagnosis of Amoebic from other Varieties of Dysentery.

The extraordinary rapidity with which very marked improvement follows the subcutaneous injections of $\frac{1}{2}$ -grain doses of emetine is of the greatest diagnostic importance, for cases of bacillary dysentery and other non-amoebic causes of the presence of blood and mucus in the stools are not, in my present experience, materially affected by the drug, although it has done no harm in them. Thus, in a case of chronic bacillary dysentery complicating kala-azar, emetine injections had no effect, and the disease steadily progressed to a fatal termination. Again, I was asked to treat with emetine a case of suspected amoebic dysentery with six to seven stools of blood and mucus daily. On examination the patient pointed to the caecal region as the seat of pain, and clinically I also thought the case to be probably amoebic, so injected $\frac{1}{2}$ -grain doses of emetine hydrobromide daily for three days, without the slightest effect on the number or character of the stools. I twice examined the stools for amoebae, with negative results, while cultures failed to separate any bacilli which would clump with either Shiga or Flexner serum. The rectum was then examined, and cancer detected high up. The failure of adequate subcutaneous doses of emetine to produce marked improvement within two or three days is, then, very strong evidence that the disease is not of amoebic origin. This specific action of emetine salts in amoebic disease alone is of the greatest interest and importance. Ever since I was the first to recognize the frequent occurrence of amoebic dysentery in India and to demonstrate that living amoebae are always present in scrapings of the walls of large tropical liver abscesses, I have never doubted the pathogenic action of these parasites. In my experience, whenever active amoebae of the *histolytica* type, including the variety described by Noc and shown by Grieg to be the common one in India, have been found in dysenteric stools (and I have almost invariably found this form only), the disease has eventually proved amenable to full doses of ipecacuanha, if not too acute or far advanced. Still, facilities and time for the microscopic examination of the stools of the large number of dysentery cases which often have to be dealt with in the tropics, are seldom available, so a simple and harmless clinical method of differentiating amoebic from other forms, such as is now furnished by the emetine treatment, is clearly of the greatest practical importance, and will also lead to the early adoption of suitable treatment in those cases, which prove not to be amoebic in nature. Moreover, it will allow of more rapid advances in our knowledge of the distribution of the two great classes of dysenteries than can be furnished by the very limited number of workers available for bacteriological researches on this subject in the tropics. We may, perhaps, also hope to hear no more doubts as to the existence of amoebic dysentery as a separate entity, such as were expressed in a recent editorial in a leading Indian medical journal.

Conclusion.

We have, then, in my method of the subcutaneous injection of soluble salts of emetine a specific treatment of amoebic hepatitis and amoebic dysentery, which is so rapidly beneficial in the latter as to be also of great diagnostic value between that and other causes of the passage of blood and mucus in the stools. Yet, strange to say, this remarkable remedy—probably the most active specific in the whole range of medicine, not excluding quinine and salvarsan—has for long been thrown away by those who pinned their faith in ipecacuanha sine emetina.

GRANULE-SHEDDING IN TRYPANOSOMA GAMBIENSE.

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THE "infective granule" in trypanosomiasis has been described by Major W. B. Fry, R.A.M.C.¹ Major Fry kindly demonstrated to me the presence of these bodies in experimental trypanosomiasis in animals, and I have continued investigations on similar lines here. As I am unaware of observations having been made on the "granule" of *Trypanosoma gambiense* in human trypanosomiasis, the following notes may be of interest.

Blood and gland puncture wet preparations from cases of sleeping sickness have been examined by the dark ground method, and the results confirmed by vital staining.

"Granules" are present in the trypanosomes—usually three or four in number. They are small, circular, highly refractile bodies, obviously within the trypanosome, and constantly swinging backwards and forwards in its long axis, the wriggling or lashing of the host causing these movements. When the energy of the trypanosome diminishes, it may be observed that the granules do not swing to and fro synchronously with its movements but perceptibly later; apparently there is an interval for the transmission of a wave, the granules lying more or less free within the envelope of the trypanosome. This activity of the granules gradually increases in the wet preparation, and is further exaggerated if the trypanosome becomes anchored by the posterior pole and exhibits lashing movements of the body and flagellum; the granules are then seen to be perpetually dancing in every direction within the body, sometimes impinging on the cell membrane and rebounding from it. I do not suggest that the trypanosome is actually trying to discharge the granule by its movements, but the process appears very purposeful, and the granules seem as if they were anxious to get free. Finally the granule succeeds in its efforts and shoots out into the surrounding medium; it has been noticed that, before being shed, the granule in many instances approaches the surface, and may actually bulge out the covering membrane.

In older preparations the trypanosomes begin to show signs of fatigue and later of degeneration; this may be due to change of temperature, but is probably the effect of the powerful light to which they are exposed. They move sluggishly and sometimes become swollen and bloated. At the same time the granules exhibit changes, both in number and size. Instead of what may be regarded as the normal three or four granules of *T. gambiense* there may be five or six; frequently one or two are larger than the others, and sometimes there are very small granules in pairs closely apposed and connected in some way, as they move in unison and the transmitted wave affects them together. (The questions arise: Is this multiplicity due to fission? and is it only the larger granules that are concerned with a reproductive process?) At this stage granules may still be extruded, but when the trypanosome becomes even less active, extrusion is very uncommon. A later stage is reached when a trypanosome loses its natural form, swells up and becomes almost circular, while still showing one or two granules which it is unable to extrude. On the other hand, a trypanosome may be seen normal in form but quite inert and not containing any granules; it would seem, however, to be exceedingly rare for a trypanosome to discharge all its granules.

The occurrence of granule shedding is quite distinct, but is, I believe, relatively uncommon in normal circumstances. It is exceedingly easy to be deceived, as in these preparations there are countless dancing bodies—haemoconia and leucocyte granules, which impinge on the trypanosome, and are flung away by its lashing movements; also it is possible for these particles to adhere temporarily to the envelope of the trypanosome, and be detached at any time by some forcible movement. The objection may be raised, How can one ever be sure of extrusion of a "granule" if this fallacy be admitted? This, however, can be met by pointing out that, if particles should adhere to the trypanosome, they cannot swing to and fro in its long axis. Again, the larger granules have been seen to escape from a mori-

bund trypanosome which was quite incapable of forcibly detaching particles, as its movements were of the feeblest character. A useful standard is to recognize extrusion of a granule only after the trypanosome has been under observation for some time and the swinging of the granules carefully watched.

When free in the wet preparation the granule seems to be rather larger than the small particles known as blood dust. It shows two forms—one circular, the other pear-shaped—not unlike a common form of poikilocyte in stained blood films. The explanation of this seems to be that it is actually pear-shaped, but when looked at “end-on” a circular appearance is presented, as the base of the pear-shaped body is nearer the observer’s eye. There is more than sufficient depth of fluid between the slide and cover-slip of a wet preparation for a small body like the granule to turn over on itself; therefore, if the granule, while circling in the free fluid, turns from the “end-on” position to a direction parallel with the slide, it displays its long diameter and is seen to be pyriform. It seems improbable that it actually changes its form so rapidly.

In the granule immediately after extrusion there appears to be no flagellum, but later it is indicated, though in gland puncture preparations it is indistinct. A point in favour of the existence of a flagellum is that very frequently there is to be seen a minute particle of blood dust, apparently attached to the granule by a short invisible filament; for some time the particle follows all the movements of the granule, but is afterwards left behind. This seems as if the particle had been attached temporarily to the flagellum, which was too delicate to show up clearly in the space intervening between the granule and the particle.

The difference from blood dust, leucocyte particles, etc., is clearly brought out by focussing. When the granule is slightly out of focus there is seen to be a very much greater disturbance of the medium round about it.

Motility is distinct. The granule may be carried along in the various currents and eddies encountered in wet preparations, but at other times it moves across or against the stream, and in open lacunae where there are no obvious currents it may be seen to progress across the field in any direction.

The dark ground illumination gives a better picture of the granule within the trypanosome, but the vital staining method suggested by Balfour² demonstrates the extruded granule much more clearly. By this means the granule within the trypanosome shows as a dark-coloured dot against the clearer cytoplasm, but the free granule, even in its earliest stages, stains well, and is seen as the small motile pyriform body turning over on itself. A flagellum appears soon after extrusion, and is a more distinct feature than in the dark ground preparations; this gives the granule the appearance on a very small scale of a tadpole with a short tail. I have never seen a flagellum showing undulations. It has been noted in a case with very scanty trypanosomes and granules that one granule lying close to a trypanosome had a well-defined short flagellum; this is evidence in favour of its early development, as it is highly probable that the granule had been recently extruded and sufficient time had not elapsed for the granule to move far away from the parent trypanosome, while the latter contained only one granule and was very sluggish, bearing a close resemblance to trypanosomes seen in the dark ground after they had extruded granules.

Motility is made very evident by vital staining, and frequently a granule has been watched making its way over half the diameter of a field.

Fresh blood preparations from various animals have been examined by vital staining, and observations made as to the presence or absence of the granule. A few of these cases may be quoted:

1. A rat, inoculated with a drop of gland juice, was examined on the eighth day; five slides were prepared, but in a prolonged search no granules were seen. This rat did not become infected.

2. Mule sent for examination as nagana was suspected. Blood examination by the ordinary method was negative on more than one occasion. After a long search through many slides (vital stain preparations) one very suggestive, though non-flagellated, granule was seen, but no trypanosomes. In view of this granule I suspected strongly that the case was positive, and the follow-

ing day, after many examinations, a trypanosome was found with an actively motile flagellated granule in the same field. This case may almost be said to have been diagnosed by the discovery of the granule at the first examination.

3. Monkey infected with *T. gambiense*. At an early stage of the case five wet preparations were made; only one trypanosome was seen, but motile granules were present in all the five slides.

4. Mule suffering from epizootic lymphangitis; granules were not seen.

In gland puncture vital stain preparations from man motile granules were never seen in a case that did not prove positive by the discovery of a trypanosome.

Granules have been found in fluid obtained by puncture of internal organs—liver, spleen, and lungs—but the number to be seen in such preparation does not seem to bear a definite relation to the severity of the gland infection. It is, I think, probable that the granule undergoes development in the internal organs, and suggestive forms have been seen. Some phenomena have also been noted after treatment. Further observations are to be made on these points.

SUMMARY.

1. The “infective granule” of trypanosomiasis occurs in *T. gambiense* in cases of sleeping sickness.

2. Granule shedding has been observed, and the free granule seen in lymph glands and internal organs—liver, spleen, and lung.

3. The granule is at first pyriform, but develops a flagellum. It is actively motile, and can be distinguished from “blood dust.”

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THE RESULTS OF SANATORIUM TREATMENT.

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In this communication we record the results of treatment and the after-histories of 1,102 patients, who passed through Kelling Sanatorium between January, 1903, and March, 1910. We think certain other facts elicited from this number of patients are also worth publishing.

Our patients have been drawn from all parts of England and Wales and the Isle of Man, but more than half of the total number came from London and Norfolk. They belonged to the wage-earning classes, and their admission to the sanatorium depended solely upon their inability to pay the fees of private institutions and upon their being certified as medically suitable. It scarcely need be said that applications for treatment have always exceeded our number of available beds, and that we have never been without a formidably long waiting list. The following information was obtained from these 1,102 patients.

Age and Occupation.

Their average age at the time of the first observed symptom of their malady was 25 years and 10 months; 718, or about 65 per cent., were town-dwellers; 384, or about 34 per cent., were country-dwellers. As regards their employment: Of the 707 men, 71.7 per cent. worked indoors, while 28.3 per cent. worked out of doors. The 372 women were, practically speaking, all employed indoors.

Family History.

A family history of pulmonary tuberculosis in the direct line was obtained from 459, or 41.6 per cent.; 363 patients stated that they had been exposed to the risk of infection from other consumptives, and 37 had occupied infected houses.

Personal History.

The vital importance of proper treatment in the very earliest stages of their disease is our reason for calling attention to the following notes.

The average time allowed to elapse between the first manifestation of the disease and application being made for sanatorium treatment was one year and six months.