Dr. BRUCE.—No, you produce no leucocytosis. It reduces the pulse and temperature. What is it you are introducing into the body? Is it the immune body? Is the patient deficient in the complement and unable to prepare his own antitoxin? It was merely with the idea of getting some suggestions as to this that I brought the question forward.

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## *The Trypanosoma of Sleeping Sickness.* By ROBERT JONES, M.D.

BY the courtesy of Sir Patrick Manson, K.C.M.G., I am permitted to show you specimens of (1) the trypanosoma from the human subject, an European, which is the first instance of such a discovery; (2) in monkey got by injecting human trypanosomes, the specimen being one, I believe, of Dr. Castellani's own preparation; and (3) the Tryp. Lewisi from the sewer rat. I make no apology for drawing attention to the possible cause of a disease—sleeping sickness—which is so nearly allied in its clinical symptoms to the condition of katatonia or hebephrenia, two of the varieties of dementia præcox which, in increasing numbers, many of us are called upon to treat. Recently my colleagues and myself have made an unsuccessful attempt at lumbar puncture in order to have examined the cerebro-spinal fluid of a case of katatonia. Let us briefly contrast the trypanosoma with the malaria parasite.

Less than ten years ago nothing really was definitely known of malarial parasites outside the human body. Now the extra-corporeal life is fully ascertained, and the co-existence of malaria with the anopheles mosquito has been fully investigated.

Briefly, the malaria parasite or the *Plasmodium malariæ* has two phases, or a dual cycle, an intra-corporeal and an extra-corporeal life.

To take the varieties of malaria, *viz.*, *tertian*, in which the *plasmodium* matures and discharges itself from a red blood corpuscle in forty-eight hours; the *quartan*, in which the same takes seventy-two hours, and the *Æstivo-autumnal*, also a forty-eight hours' maturity. In all these (1) after a chill, the red blood-cells contain highly refractile and actively amœboid small bodies, which are the early forms of the plasmodium and are

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called *Merozoites*, which form a small ring around a central clear space; (2) some hours later granules of pigment appear in these forms, and the pigment granules are motile; (3) at intervals, for forty-eight hours, these plasmodia occupy the whole of the red blood corpuscles, which are pale, owing to the destruction of the hæmoglobin; (4) in forty-eight hours all amœboid movements cease, and the nuclei, of the segmenting mature forms, become visible; (5) finally, the cell bursts, an infinitesimal number of small merozoites—each with a nucleus—is set free to enter other blood-cells. These again mature in forty-eight hours and discharge themselves, once more to re-enact the cycle. This process describes one cycle only.

Co-existing with these granular forms are crescent-shaped bodies with pigmented centres, but without amœboid movements. These bodies have sexual capabilities, that is to say they have the power to prolong and perpetuate the species in a cycle outside the human body. They do not segment into *merozoites* but remain circulating in the blood. When out of the blood some of the forms ex-flagellate, *i.e.*, throw out and eventually set free a long *flagellum* which enters other cells.

Each flagellum contains some of the nuclear chromatin of the organism from which it arose. This flagellar chromatin unites with the chromatin of the cell into which it entered.

The result of this union is a *zygote*, which divides into *zygotomeres*, and the formation of *zygotoblasts* or *sporozoites*.

This process was observed to take place within the body of a special kind of mosquito—the anopheles. No other fly is known to act as *host* to the *plasmodium*.

After some time within the mosquito, the sporozoites find their way into the salivary gland and into man, in whose blood the sporozoites either become the amœboid forms or the *merozoites*. The crescents may develop either within the mosquito or elsewhere *outside the body*.

Two types of cells develop in the sexual cycle, the male cell, called the *micro-gametocyte*, out of which grow flagella, called the *micro-gametes*. These enter the other larger cell—the female—called the *macro-gamete*. All these enter, grow and mature in the red blood corpuscles, and are *endo-globular*. When quinine is administered it destroys first of all the amœboid forms, the sexual form being more resistive.

The special feature of malaria is that the *plasmodium* has two

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cycles, one of which is completed in the body of the mosquito. Not so with *Trypanosomiasis.*

The *Trypanosoma*, so far as is known, has no separate cycle within a fly—the tsetse fly (*glossina palpalis*). This fly only acts as a carrier, and is thus different from the anopheles of malaria.

As to "sleeping sickness" of which the trypanosoma *may* be the cause, it was first known in the Congo or the back country of the West Coast of Africa. It was scientifically unknown until 1901, when Dutton found trypanosoma in the blood of a European suffering from a peculiar combination of symptoms, described as tropical disease. This was published in 1902. Later the trypanosoma was found in a blood film taken from a native child in the Gambia. A second case caused the Liverpool school of Tropical Medicine to send Drs. J. E. Dutton and J. L. Todd, in 1903, on a research expedition to Senegambia, and their report was published the same year.

They found that the trypanosoma varied in distribution and prevalence, that it was more prevalent in the rainy season, and near rivers. Many who were attacked were listless, and some had fever. Further observation revealed the fact that the disease attacks especially the negro race, that hundreds of slaves died of it in plantations or on board the transport ships. A few of the half-breeds appear also to be susceptible to it, and the disease has been known in the case of two or three Europeans—a notable instance being the recent death in London of the wife of a missionary from sleeping sickness.

Recently the disease has spread into East Central Africa, especially up the Nile and into Uganda, where entire villages have been depopulated. In one province—Busogo—30,000 natives died within the last three years, and in another district on the shores of Lake Victoria Nyanza, Dr. Nabarro stated that 50,000 deaths were caused by it last year alone!

In 1902 the Royal Society commissioned Drs. Low, Christy, and Castellani to investigate the disease in Uganda. Manson, however, had worked out two or three cases of Congo sickness which were sent over for accurate investigation, and he held some suspicion that the cause might have been the nematode Filaria perstans, which was common in South America and the West Indies, but no sleeping sickness was known to occur in any of these areas. The result of the 1902 expedition of the Royal

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Society (the proceedings of which, through the courtesy of Sir John Evans, are before us) resulted in Dr. Low finding that Filaria perstans was not a cause, in Christy pointing out the geographical distribution—the North East Coast, and the islands of the Lake, and in Castellani finding trypanosoma in the cerebro-spinal fluid in 56 *per cent.* of cases of sleeping sickness. Low and Christy returned, and Castellani remained. The Royal Society, in conjunction with the Foreign Office, sent out a second Commission, Dr. Bruce (who had previously discovered the blood parasite of nagana, the carrier of which is the tsetse fly), and Dr. Nabarro. The recent proceedings of the Epidemiological Society have made the findings of these investigations public property.

The conclusions are that trypanosoma is extensively found in the blood of non-sleeping sickness cases—every third or fourth native has it—but in addition is found in the cerebro-spinal fluid also of all cases of sleeping sickness, but not in trypanosoma fever; that streptococci and diplococci are also found in some of the later stages; that the lymphatic system is greatly affected, and that there is much similitude between the map of the tsetse fly and that of the area of sleeping sickness. There are "fly belts" and "sleeping sickness belts," though there are plenty of tsetse flies in some places without sleeping sickness; the areas of both are forests near the water's edge, dense undergrowth—not swamps like malaria, and not grassy plains. The tsetse fly does not follow big game; it may be on one side of a river and not the other, also air-breathing fish may contain the fly.

The disease certainly has a long incubation period, and two, three, or five years after the person has left an endemic centre, he may fall a victim, as in hydrophobia. After onset, the disease makes rapid progress, and is mostly of three or four months' duration. Death is hastened by inanition, pneumonia, dysentery, or septic bedsores.

The symptoms are a slowly increasing and insidious drowsiness. The patient is languid and taciturn, slow and dejected, dull, listless, and has an overpowering lassitude. Occasionally there is a sense of weight or pain in the head, and there may be giddiness. The patient can be roused, and then replies in monosyllables, but correctly. He can stand, but with tremor. There is no definite knowledge of time or place with him.

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Food collects between the cheeks, and the urine and motions pass involuntarily.

The chief pathological condition in the brain is a collection of lymphocytes in the peri-vascular lymphatic channels, which cells are said to withdraw the oxygen otherwise meant for the neurons.

As to the trypanosoma itself, I hand round the four reports of the Royal Society, and the joint paper of Drs. Rose Bradford and Plimmer in the *Quarterly Journal of Microscopical Science*, the latter showing the special trypanosoma of the London sewer rat, and I here express my indebtedness to Dr. Plimmer for his trouble in giving me personally much information.

The trypanosoma has (1) a micro-nucleus; (2) a macro-nucleus; (3) an undulating membrane which all stain with erythrosin; and (4) a vacuole and a flagellum. As to the multiplication of the rat trypanosoma, that of the conjugation of two cells is one method; the micro-nuclei fuse and then divide, and the division appears to be more vigorous after conjugation. The second method appears to be analogous to that of the plasmodium, with amœboid movements. A bunch or tangle seems to be formed in which the micro- and macro-nuclei mix together, and then amœboid bodies are thrown off, from which it is not quite certain, but it is surmised that the complete trypanosoma grows. Phagocytes are seen to attack the amœboid forms, and the plasmodium may, by blocking up the vessels, produce stasis. It is interesting to note that although the multiplication of these lower organisms appears to be in a great measure by fission, they may multiply by conjugation, which appears to reinforce their vitality. The division of the *Paramœcium* was watched by Calkin until fission had taken place to seven hundred times, after which there was no further vitality to reproduce itself in this manner.

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*Notes on Adolescent Insanity in Dorset.* By GEORGE A. RORIE, M.B., Senior Assistant Medical Officer, Dorset County Asylum.

CONSIDERABLE attention has recently been directed by several observers to adolescent insanity and dementia præcox,

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