

Original Articles.

A PRELIMINARY NOTE ON A PYROPLASMOSIS FOUND IN MAN AND IN SOME OF THE LOWER ANIMALS.

BY A. LINGARD, M.B.,

Imperial Bacteriologist to the Government of India; and

E. JENNINGS,

MAJOR, I.M.S.

IN 1902 hæmoglobinuria of cattle due to the presence of the pyroplasma bigeminum* made its appearance in plains cattle at the Bareilly Laboratory after the subcutaneous inoculation of rinderpest blood. In the injected cattle, the symptoms of the second disease followed before those of the primary one had disappeared. The injected blood was found to be free from the parasite, and no other cattle out of some 90 inoculated showed symptoms of any disease but rinderpest. It was therefore pointed out that the organism is able to lie dormant in the system of some of the plains cattle of this province, until such time as the restraining power present in the blood has been modified, or removed, when it again assumes an active state. Further, the reduction or entire removal of the hereditary or acquired resistance to the pyroplasma bigeminum may, in some cases, be materially hastened by such animal passing through an attack of any other febrile disease, which brings about depressing conditions. Whether the years 1902-1903 were exceptional ones in the plains of India we are not as yet in a position to say, but all animals which have come under observation of whatever species, with the exception of bovines and buffaloes received from the Himalayan regions at Muktisar, and these at times may perhaps be carriers of the same, have without exception respectively exhibited pyroplasmata in their red corpuscles and free also in the plasma. Further, all Himalayan animals, bovines and buffaloes, after coming across the Bhabar and Terai regions, belts of land lying between the foot of the outer Himalayas and the Bareilly district, have exhibited the same organisms. The presence of these pyroplasmata are not confined to the Bareilly district, but are more or less scattered over a large area of North India; the following facts indicate:—

Shamsher and *Kilogarth*, an Arab and a T. B. English stallion respectively, brought the organisms in their blood from the North Punjab. Three mares, railed direct to Kathgodam from Hapur Remount Depot in May 1903, exhibited the organisms in their circulations

a few days after their arrival at Muktisar. Donkeys taken to the Hill Laboratory in July 1903 exhibited the same parasites in their blood shortly after their arrival. Specimens of blood from brood mares suffering from surra, and guinea-pigs inoculated with blood from affected animals in the Maindot State, Punjab, all exhibited the same form of organism in their respective circulations. Up to date the following animals have been found to be the subjects of spontaneous pyroplasmosis in Bareilly:—

1. Bovines, plains and hills animals.
2. Buffaloes " "
3. Equines, English, Australian Arabs, country-bred horses, "tatoos" and donkeys.
4. Elephants.
5. Camels.
6. Goats and kids (latter a few weeks old).
7. Sheep, from Bareilly district.
8. Dogs, English and pariahs.
9. Cats, tame and wild.
10. Monkeys.
11. Several species of deer.
12. British breeds of fowls.

White rabbits, guinea-pigs and rats (*m.d.*) have been inoculated with the pyroplasmata. The blood of an eighth month foal born dead, the mother a hill pony, exhibited all the different forms of the asexual variety of the pyroplasma in the red corpuscles and blood plasma, in addition the blood of a donkey foetus, about the fifth month, contained the organism. So that the parasite is capable of passing from the maternal to the foetal circulation through the walls of the placental vessels.

It would appear probable that man and animals alike in certain seasons, may all present the same species of pyroplasma, but modifications in the specific characters of hæmatozoon are developed during the passage through the different animals.

Smith and Kilbourne proved that ticks are the carriers of the pyroplasma bigeminum from one season to the following, and young ones hatched out from the eggs were capable of conveying the disease to any susceptible cattle they attach themselves to. Koch has shown that young ticks placed on blades of grass on the veld are but little influenced by the exposure to wind and weather, the young ones huddle together at the extremity and under-surface of the blades of grass, ready to transfer themselves to any animal which comes in immediate contact with them, and further the same breed of bovines which were incapable of contracting the pyroplasma by the inoculation of infected blood, readily took the disease spontaneously in a severe form when exposed to the bites of infected ticks on the veldt.

Here then we have one way explained as to the means by which the pyroplasma is carried over from one season to another in animals. But man is not infected with ticks except under

* The spelling of the word, pyroplasma or pyroplasma, is uncertain and should be agreed upon.—ED., I. M. G.

exceptional circumstances, and therefore it becomes necessary to search for some other species of carrier. Our attention was naturally turned to the culicidæ and the biting forms of the diptera, but in the cold season but few if any of the latter species are to be found.

As before mentioned culices were present in force during January and February for they began to hatch out in December, and *C. Fatigans* and *C. Annulatus* were very numerous, especially the former variety.

On examination of stagnant and dirty water from puddles which were left, dried up after the *pucca* monsoon and also those after the winter rains, the parasitical elements of the disease were found in large numbers, although they were not present in recently fallen or running water, but in puddles which dried up and later re-formed after a further fall of rains, the elements of disease were nearly always forthcoming, so that neither cold nor dessication destroys the parasitical elements.

Further in the eggs, larva pupa and *C. Mosquitoes*, obtained from dirty water puddles, the parasites in one form or another were frequently demonstrated. The larva took in other low forms of life as food, and contracted the parasites from them or are carried over to them in the eggs, as in the case of the tick. The parasites were also found in anopheles mosquitoes, but too late to act as the intermediate hosts, for they were not present in January and February and were only hatched out in the middle of March and then only in small numbers, the first being discovered this year on the 15th of March.

The question as to *Culex* causing this disease in man has been gradually forced upon us, for two years ago, out of a population of 2,500 souls at least 1,800 during January and February were the subjects of fever, not of a severe type, but quite sufficient to make the patients feel miserable and unfit them for work. During the presence of this fever anopheles mosquitoes were as rare as the "Dodo" in Bareilly, and although diligently searched for and relatively large rewards offered for them none were forthcoming. At this period of the year *Culex* were swarming, and as quinine had no effect upon the course of the disease other means had to be found and employed. What checked the epidemic was burning "uplas" at night and causing a dense smoke which drove the *Culex* away. This year test experiments were instituted, and in those rooms where "uplas" were burnt, the proportion of cases attacked were extremely small in number as compared with those which occurred in rooms where the "uplas" were not burnt.

Further in February 1903 a Gwalla, a *Pahari*, suffered at Bareilly (during the prevalence of Texas fever in cattle with hæmoglobinuria as a marked symptom) benign tertian, associated with the pyroplasma, during which serious symptoms of a remittent type of fever

were developed, together with intermittent attacks of hæmoglobinuria lasting for over three weeks in all.

Symptoms in man.—The disease appears to come on in an insidious manner; a patient in apparently good health, within a period of some months, may present a sodden and pasty condition of the skin and an appearance of marked anæmia and cachexia. In ordinary cases the patient complains of headache, frequently hemicrania, the temperature is sometimes normal or subnormal in the morning, while in the evening it may rise to 99° or 100° F. as a maximum, a general feeling of malaise and sweating on the slightest exertion. At times some yellowness of the conjunctivæ may be noted, while the urine in severe cases exhibits on occasions a smoke tint, and red corpuscles are found on microscopical examination or hæmoglobinuria alone is present. In advanced cases granular and hyaline casts have been observed. In the cases which have come under observation the spleen and liver have been found to be normal in size, or only very slightly exceeding the normal proportions. Further no pigmentation of the skin of the cheeks or extremities has been noted, and the organisms invading the red corpuscles of the blood are devoid of pigment. One marked feature the temperature charts exhibit, is the presence of undulating curves at intervals with normal or subnormal temperatures intervening.

Symptoms in animals.—The great majority of mammals in this country must possess more or less protection against this form or forms of pyroplasmosis, for up to the present no animals have been obtained either in Bareilly or from other districts in whose blood pyroplasmata in some form or another have been found absent. It is somewhat difficult to say what stages, if any, the animal passes through in the first instance, if born free from the parasite.

When apparently healthy animals have their temperatures taken and recorded morning and evening, but slight variations are noted, whereas bovines injected subcutaneously with acute rinderpest serum, or with virulent rinderpest blood, may either develop a severe form of pyroplasmosis and in course of time succumb, or in the event of a modified form occurring, the temperature curve shows undulations at intervals with no other symptoms. Equines presenting pyroplasmata in their blood for long periods may show no variations from the normal temperature, then suddenly an undulating curve lasting from 5 to 8 days is observed, even when horses and donkeys with pyroplasmata in small numbers in their circulations are inoculated with either the bovine or the *Surra* Trypanosoma respectively. The former organism would appear to produce but a slight effect on the health of the inoculated animal, certainly during the course of the concurrent diseases, symptoms may become manifest, and it is at times most difficult to know to which

parasite the changes are referable. In European breeds of fowls introduced into this country, the pyroplasma would appear to bring about attacks of marked fever, for during the period of the greatest invasion of the organism the following symptoms are present:—anorexia, head hanging down, drowsiness, comb purplish in colour instead of bright red as in health, drooping of the feathers, malaise and general indisposition.

Lizard (Common Indian variety).—During the cold season and later the blood of lizards caught in the bungalow were found to be free from the pyroplasma, but when the mosquitoes appeared in large numbers, lizards caught on the verandah outside the house presented the organism in their circulations, and after the mosquitoes had entered the building the blood of the lizards caught inside the building were also found to be invaded.

Inoculation of a lizard whose blood was free from the parasite.—The larva of an infected *Culex fatigans* in which both micro- and macro-gametes were present in large numbers, was mashed up and triturated in sterile distilled water, and five minims of the mixed fluid injected subcutaneously into a lizard free from the parasite. In 24 hours after inoculation, the red corpuscles were found to be free from microgametes. The female cells were either replete with elements or had already evacuated their contents. Cells containing the male elements, and others, the walls of which had given way, were observed. The latter exhibited masses of gelatinous material from which the dumb-belled bodies were wriggling and liberating themselves in the plasma.

In 48 hours some red corpuscles contained the elements of one sex only, while others exhibited both male and female elements. Further several cells containing very small pyroplasmata were noted in an early stage of development. The different stages observed in the latter were: (i) two small black dots surrounded by a halo; (ii) the dots lying rather further apart; (iii) dots slightly turned upwards; (iv) semi-lunar in form with enlarged ends; (v) still larger in size; (vi) the pyroplasma in pairs connected probably by their bases.

In 72 hours the pyroplasmata had become developed within the red cells, while large numbers of others were seen free in the plasma. The female elements in the red corpuscles had increased in size. Male and female elements were free in the plasma, and present in the cells in considerable numbers.

During the second cycle of 72 hours, between the 4th and 6th days inclusive in stained specimens (Modified Romanowsky's method), in addition to the changes noted above certain others were observed. (a) Small bodies invaded the red corpuscles between the nucleus and its outer margin; they stained a reddish-purple in colour and gradually increased in dimensions until they ruptured the red corpuscles in which they

were situated, they then developed what appeared to be vacuoles in their interiors, and later the contents of the cells escaped, but the mother cell still maintained its position in proximity to the red corpuscle, although a slight space between the cell and the red corpuscle could be detected. The liberated elements appeared to be micro-gametes. (b) Other red corpuscles were invaded by cells which stained a purplish red, which, when mature, presented somewhat the appearance of mulberries. It was considered probable that these cells contained micro-gametes. (c) A third form of cell developed within the red corpuscles; these stained a dark red, were somewhat circular in the first instance, but later increased and assumed irregular forms, more or less globular; before leaving the red corpuscles and escaping into the blood plasma they developed vacuoles in their interiors, which at first could be only just made out, but which later increased in size until they became a marked feature. (d) Large mononuclear lymphocytes, with nucleus stained purple and body of cell a light blue, contained numerous bright red-coloured bodies in their interiors, the greater number in the protoplasm of the cell, although a few were observed in the interior of the nucleus. These red-coloured elements resemble micro- and macro-gametes, for some are circular, while others present dumb-bell forms. These elements would appear to have been taken up as foreign bodies, the cell for some reason having taken on the duties of a phagocyte.

Mosquitoes and Ticks.—The gametes are of two sexes: the male element, or microgamete, appears to consist of a dumb-bell shaped body, supplied with cilia, for when two male elements come together, the extremities do not come into opposition, but appear to be separated by a kind of halo, which surrounds the extremities. It is endowed with movement, twisting, and twirling. When in the horizontal plane it presents two beaded extremities, with a short connecting rod, whereas when in the perpendicular plane but one globular extremity is visible, and can be seen as a black speck. The female element, or macrogamete, presents a circular form, is translucent, and considerably larger than the male. No nucleus or other structure can be observed. In fresh specimens the body is endowed with movement, and therefore probably possesses cilia also.

When the male and female elements are free *in vitro*, prolonged observation under the microscope will reveal the male, executing a series of movements round the female, evidently with view to discover a means of entrance in the female element. The search may occupy in some instances a considerable period exceeding an hour, in others, but a few minutes. When the object of the search has been discovered the male makes a sudden dart and would appear to enter the female by means of an existing

duct or passage, for instantly the male is seen within the female element and as suddenly all movement ceases, and the male element becomes stationary. In this way the zygote is formed. From this point the description must diverge according to the changes which have been observed in the zygote, whether for the development of the micro- or macro- gamete.

Macrogamete.—A small body is observed in the lower segment of the zygote somewhat semilunar in form, but with rounded extremities; this body gradually increases in length and general dimensions, until it occupies $\frac{1}{2}$, $\frac{3}{4}$ and $\frac{7}{8}$ of the circumference of the cell, the centre remaining free. At this period of the developmental stage certain bodies, somewhat circular in form, are first observed in the annular body, which later become well defined and complete the ring, while still the centre remains free. Still later the small circular bodies become free within the cell and occupy all parts of it, including the central portion. The cell now distended, gives way, and the contained bodies leave the cell in a mass of gelatinous material, and free themselves in the plasma. These are the macrogametes.

Microgametes.—The development of the male elements from the zygote would appear somewhat analogous to that of the macrogamete. As the zygote increases in size it appears to contain a small central mass, surrounded by clear protoplasm, while a narrow band round the inside of the circumference of the cell contains a very fine granular material. As development proceeds the central mass gradually increases in size, until it presses and encroaches upon the external ring containing the fine granular material. At this period the central mass appears to be made up of short bodies endowed with movement. When mature the cell bursts and sets free dumb-bell shaped elements which are at first entangled in a gelatinous mass, wriggling hither and thither until they liberate themselves and become free in the plasma.

Ticks.—The mode of development of the parasite in the tick appears to be analogous to that in the mosquito. A female tick, distended with blood, was removed from the ear of a pariah dog, and allowed to remain in a small sterile bottle for a number of weeks, until it had become quite dry, shrivelled and dead. On dissection, and when a small drop of sterile water was placed upon the internal organs, left for half an hour, well covered, and subsequently examined microscopically it then exhibited the presence of innumerable micro- and macrogametes. Further ticks taken from Hill bovines in January 1903, which latter had been brought from the mountains across the Bhabar and Terai in December 1903, deposited eggs in sterile test-tubes. The eggs after a period of over 60 days, when crushed and triturated in sterile salt solution and left for some minutes, also revealed the presence, on microscopica

examination, of micro- and macro- gametes in some numbers.

In man.—In mammals, including man, the development of the pyroplasma is of the asexual variety. Both male and female elements enter the red corpuscles, the after changes being more or less of the same character. The female cell, presents, in the early stage of development, a small curved body in its lower segment, which by successive stages, extends and occupies some $\frac{2}{3}$ ths of the circumference of the cell. Ultimately the annular body forms a complete ring and presents a number of circular bodies situated in regular order round the circumference of the cell; when mature the mother cell bursts and liberates a protoplasmic mass, containing small cells circular in form. As each individual cell leaves the mass an excavature, or bay, is left in it, corresponding to the size of the cell just released. Further, each of the liberated round cells commences to develop and gradually increase in size until they become fully matured, burst and set free small round transparent cells, which are the macrogametes.

Shortly after the male element obtains an entrance into the red corpuscle, the terminal enlargements grow further apart so that the connecting bar between the dumb-bell is lengthened. The poles then exhibit indications of turning up, this condition gradually increases until fully developed pyroplasmata are formed. Next the pyroplasma becomes liberated from the blood cell, and later the nucleus, or karyosome, is shed by the mature parasite. It is conjectured that the karyosomes, when free in the plasma, gradually increase in dimensions until when ripe, they in their turn, burst and set free the microgametes.

In the lizard it would appear that both forms of development, *viz.*, the sexual and asexual, proceed concurrently, while in mosquitoes the sexual form is present, and in man and in warm-blooded animals the asexual only.

This preliminary statement of the investigations, as observed up to the present, is simply being put on record, as one of us is proceeding on leave.

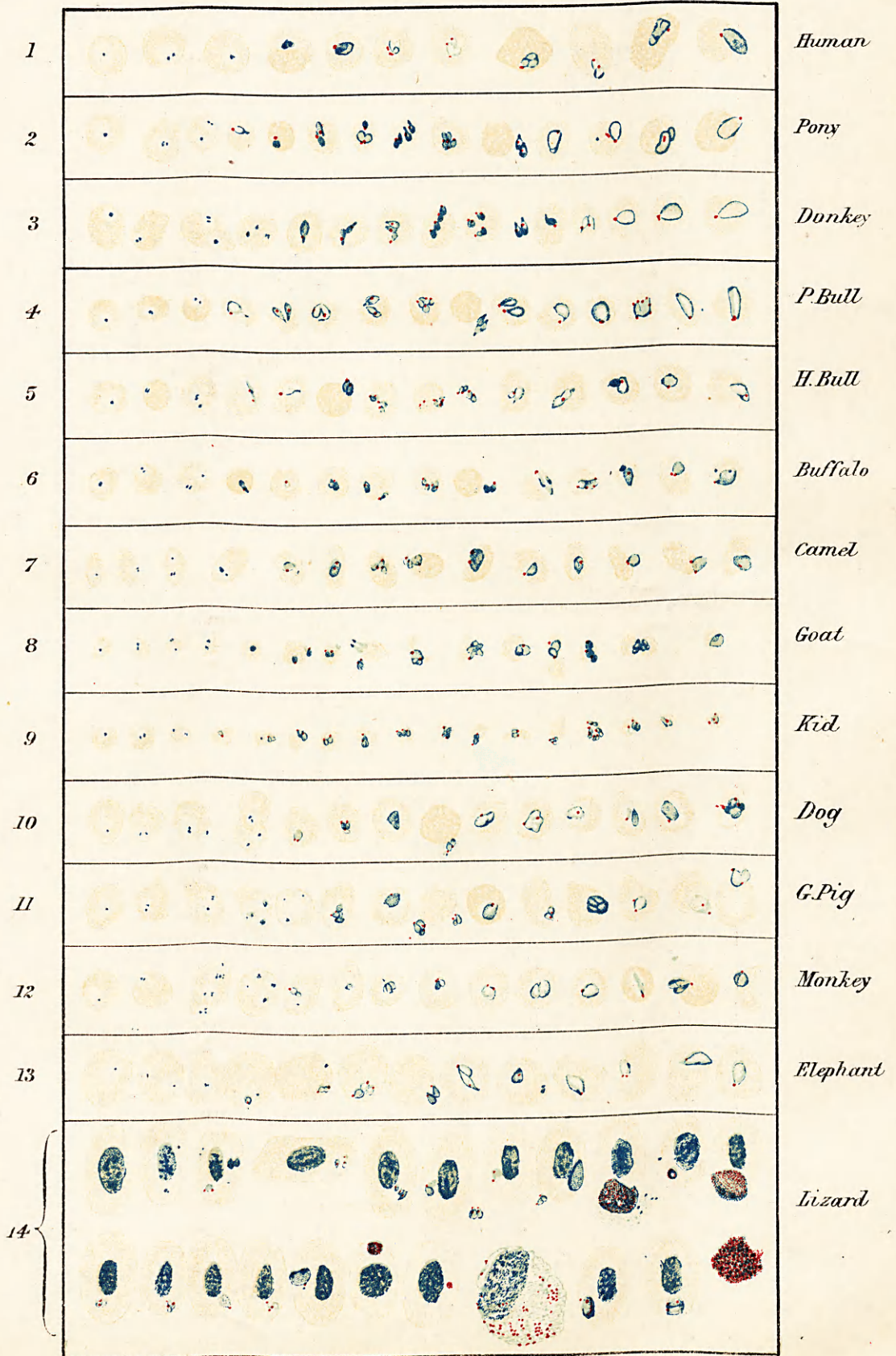
The observers, however, reserve to themselves the right of adding to, or withdrawing, any views which have been expressed, and which may later be found to bear a different interpretation when further researches have been concluded. It is thoroughly recognised that only the threshold of this enquiry has been entered and that much remains to be confirmed of what has been observed, whilst innumerable new facts remain untouched. The unification, or differentiation, of the organism observed in various animals must engage attention in the near future, while questions with regard to the symptoms produced by the pyroplasma in man in different parts of this country are of primary importance, with a view to determine if diseases like *kala-azar* and other cachexias, the intimate etiology

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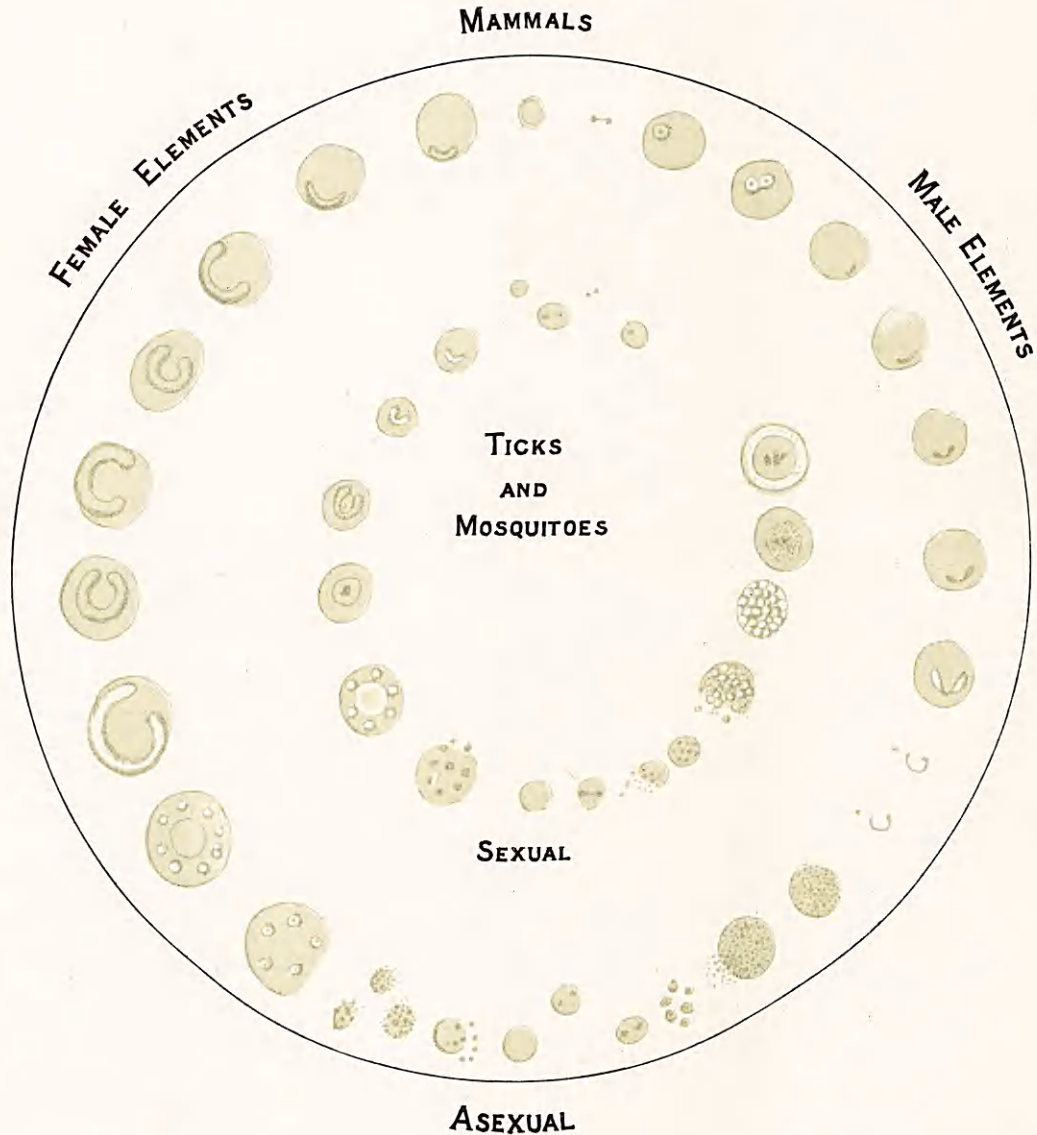


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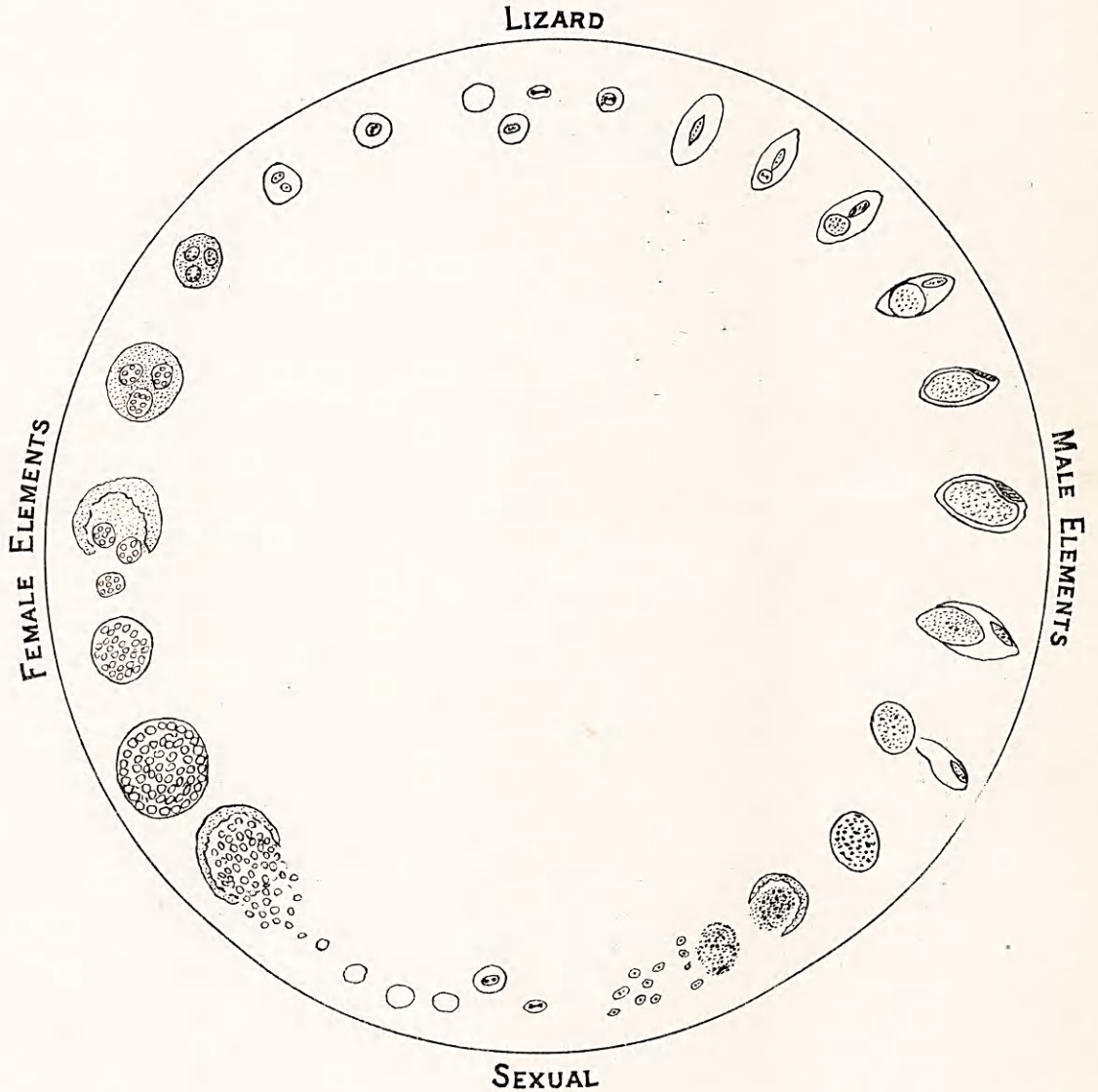


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of which are now but little understood, may not be in some way connected with this or some modified organism belonging to the same genus.

EXPLANATION OF ILLUSTRATIONS.

Magnification of all red corpuscles 1000 diameters.

Plate I.—Red blood corpuscles of various animals showing the early and mature forms of pyroplasmata within the cells.

No. 1. Human red blood corpuscles, 2. Pony. 3. Donkey. 4. Plains bovine. 5. Hills bovine. 6. Buffalo. 7. Camel. 8. Goat. 9. Kid. 10. Dog. 11. Guinea-pig. 12. Monkey. 13. Elephant. 14. The lizard.

The first corpuscles in each line respectively, show the male elements in the red corpuscles, depicted as small dots, one pole only observed, surrounded in each instance by a halo.

The second corpuscles showing two small dots, with a connecting bar between, which is more or less invisible, the horizontal position of the former also presenting a halo.

The fifth corpuscle of No. 4, Plains bovine, depicts what appears to be the veritable pyroplasma bigemnum.

The fourth corpuscle of No. 5, Hill bovine, shows the bacillary form of the pyroplasma, so frequently observed in the blood of plains cattle in these provinces.

In the other corpuscles of various animals depicted, it will be observed that the pyroplasmata have taken a blue stain with the karyosome or nucleus red in the early stages of development, but as the organisms attain larger proportions or are more advanced in age and development, but a faint blue colour is retained, although in most instance the karyosome stains red.

In the red corpuscles of the lizard, different forms of organism have been depicted, both developmental and mature forms of the pyroplasma.

Microgametocytes—7 and 6 of line 2 and 11 of line 1.

Macrogametocytes—11 of line 2, with red elements.

JAIL STOMATITIS.

By NOBIN CHUNDER DUTT,

Civil Surgeon, Palamau.

NEXT to dysentery one of the most prevalent diseases in some Bengal jails is a kind of ulcer affecting the gums, mouth, tongue and the fauces. This has, for many years, been regarded as scurvy or a disease of scorbutic origin. Major W. J. Buchanan in his excellent little book on *Jail Hygiene*, after describing its appearances says: "The present writer, however, in common with nearly all medical officers in Bengal who have commented upon these appearances does not believe that they have any connection with

scurvy, but they are due to malaria," and he has given the following reasons for this opinion:—

1. The appearance of the symptoms coincides with the most malarious portion of the year (*i.e.*, end of the rainy season).

2. Frequent history of repeated attacks of malarial fever.

3. In malarious years this condition is frequent.

4. In jails, where undoubtedly a good and sufficient quantity of fresh vegetables has been issued, and in which fresh meat was also frequently given, the condition has appeared in malarious years.

5. Failure of lime juice treatment to remove this condition.

6. Absence of effusion and ecchymosis of blood.

That the disease is not scurvy or of scorbutic origin is now settled; but what is it, and is it entirely due to malaria?

I venture to submit to the readers of the *Indian Medical Gazette* the following facts which have come to my notice during the last two years during which I have studied this disease as it presented itself to me in the Daltonganj Jail for whatever they are worth.

This disease has been of yearly occurrence in this jail from the very beginning of its existence. Except a few of the most aggravated cases which were treated in hospital no records of any others had unfortunately been kept during the past years. I took over charge of the jail about the middle of September 1901 with a legacy from my predecessor, of a somewhat large number of these cases* in various degrees of development amongst a jail population of 115 of all classes. A careful record was however kept during the years 1902 and 1903. The first case in 1902 appeared on the 16th of June, 65 others quickly followed—39 amongst the convicts, and 27 among the under-trials. By the middle of October they had all been cured, and no new cases occurred during the remaining portion of the year. Of all the diseases in the surgical nosology this bore the closest resemblance to what is known as stomatitis in almost all its different varieties, namely, herpetic, aphthous, ulcerative and even mercurial, except the gangrenous, which is generally known to us as cancerum oris, and is, I believe, exclusively of a malarial origin, being almost invariably found co-existent with an enlarged spleen and an extremely debilitated and shattered constitution. Some of the cases in the Daltonganj Jail began as herpetic or aphthous variety and developed into the condition bearing every resemblance to the mercurial, with foul breath, swollen tongue, spongy gums, salivation, swelling of the parotid and submaxillary glands and loosening of the teeth.

* The exact number unfortunately cannot be given, but if I mistake not nearly one-third of the jail population.