find out the cause of the high pressure, such as errors in diet, alcohol, syphilis, lead, and excessive worry, remembering that supernormal pressure is not a disease *per se*, but a symptom only. If the left ventricle is hypertrophied it suggests the pressure has been persistently high for some months or years. Experience teaches us that with a restriction of red meats and alcoholic drinks from the dietary of those who take them freely the pressure, if not a permanently high one, usually diminishes, and this argues that purin bodies and alcohol probably act as vasoconstrictors. Waste is constantly going on in the body, and it is important to get rid of the products of waste whatever they may be. The proof of the splanchnic vessels being some of the earliest to become affected in arteriosclerosis points to our relieving congestion of the visceral vessels, which can be done by judicious purgation, and 1 gr. doses of calomel and saline purgatives are most useful two or three times a week. One of the greatest outlets for waste products is the skin, and when inactive a free action of this organ must be encouraged by artificial means, such as by massage-douche and Nauheim baths, when these can be obtained, and intestinal lavation is also very desirable in cases with constipation. It is a common observation that with a dilated periphery causing an active skin we have a lower range of blood pressure, which leads us to suggest to those who can afford it to follow the sun. The cardinal principles of treatment, then, resolve themselves into a strict regulation of the intake and an active outlet for the waste products, and moderate exercise followed by rest is very desirable to give a better distribution of the blood. In all cases observations must be made with the sphygmomanometer from time to time as a guidance in treatment.

If in spite of our *régime* and treatment the pressure continues high after having watched the case carefully for some months, we conclude that this is a case in which the pressure is permanently supernormal. In any case, we recommend the general *régime* to be continued, and so long as no urgent symptoms arise the patient may do his work in life if he avoids excitement and sudden strain. Lastly, we must not use any *active* means to reduce the pressure, remembering that it is probably an advantage and necessary that the pressure should be high for the maintenance of an adequate supply of blood to vital organs. As for drugs of the vasodilator type, I mean the nitrite group, I use them very little except in emergencies, for I believe it is sounder treatment to get rid of the bodies in the system which contract the periphery by the means I have mentioned, rather than by dilating up the blood-vessels with the offending poisons still intact. I give iodides very carefully, if at all, but if there is any syphilitic history they may be pushed. As for gypsin, this I have given a trial in some cases, but with no marked results.

Harrogate.

PROTOZOAL-LIKE STRUCTURES IN THE BLOOD IN A CASE OF BLACK-WATER FEVER.

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THE cause of blackwater fever still remains one of the most important problems unsolved in tropical pathology. A friend of mine, aged 28 years, who had never had an attack of blackwater fever, arrived in England on Dec. 23rd, 1911. He had resided in Rhodesia for four years and had enjoyed comparatively good health. On Dec. 27th, after a dance, he passed blood-stained urine, and shortly afterwards had rigors, bilious vomiting, and a temperature of 104·2° F. He passed through an acute attack of blackwater fever. The urine on the fifth day became quite normal, but he collapsed, sank into a comatose condition, and died on the sixth day. Throughout my attendance upon him I took numerous blood films and fresh cover-glass preparations. The films were stained with Leishman's stain, or with Leishman's first and then with Giemsa, or fixed in absolute alcohol and stained in the usual way with Giemsa's stain. The fresh preparations were examined very shortly after they were made by ordinary and by dark-ground illumination.

Examination of the Blood.

No enumeration of the cellular elements was made during this short illness, and the hæmoglobin was only estimated once, on the last day, when it proved to be 14 per cent. The following tabulated statement shows the percentage of the leucocytes during the illness:—

	Dec. 27th, 1911. 12 noon.	28th, 12 noon.	28th, 6 P.M.	29th, 12 noon.	30th, 12 noon.	31st, 12 noon.	Jan. 2nd, 1912. 3 P.M.
	%	%	%	%	%	%	%
Polymorphonuclear ...	74	68	65	63	61	64	47
Lymphocytes... ..	12	19	21	10	15	14	20
Large lymphocytes ...	12	12	13·5	27	23	20	28
Eosinophiles	2	1	0·5	0	0	0·5	1
Myelocytes	0	0	0	0	1	1·5	4

The leucocytes were apparently about normal in number during the first three days. Thereafter they increased, and on the last day on which films were taken there was a very pronounced leucocytosis. Some few of the leucocytes contained small vacuoles in their protoplasm on the first day of the fever, a condition not uncommonly met with in several pathological states of the blood. In addition to these, one or more large vacuoles, as large in some cases as a red blood corpuscle, were not infrequently seen, especially in the last stage of the disease, and two or three most perfect examples of leucocytes containing a red corpuscle in their interior were found. One of these erythrophagocytic leucocytes was a polynuclear, the other a transitional form of white cell. The red blood corpuscles were in the first stages of the fever fairly normal in size, shape, and staining reaction, and remained more or less so till about the fourth day of fever, when moderate signs of anæmia became evident and a few nucleated red corpuscles were found. Basophilic and polychromatophilic degeneration of the corpuscles, although occasionally seen, was very infrequent at this stage. On the last day (Jan. 2nd), however, when the hæmoglobin had fallen as low as 14 per cent., all signs of degeneration alterations in red corpuscles were abundantly evident, and the blood picture was not at all unlike that seen in advanced pernicious anæmia, with the exception of the marked leucocytosis. A very conspicuous feature now was the large number of nucleated red blood corpuscles of all sizes, many showing signs of mitotic division. Whilst counting in the stained films 100 leucocytes I met with no less than 16 nucleated red corpuscles of various sizes.

So-called ring bodies described by Cabot and others were numerous in the films taken on the last day. Red blood corpuscles, often showing polychromatophilic degeneration, were seen containing red stained rings in the form of complete circles, figures of 8, or other weird shapes. These are commonly met with in many forms of severe anæmia. Free rings straightened out into threads, and staining a deep red with Giemsa's stain, were commonly seen. But what I had not previously observed in other severe anæmias was the presence of long threads of a deep red colour entering into or coming out of the bodies of lymphocytes or nucleated red corpuscles. One in particular I photographed. I should think it was a nucleated red cell having a diameter of 12μ, with a nucleus measuring 7μ. Running into this or from it was a deeply red-stained thread thicker in the middle, measuring 39μ in length, of which the part outside the cell measured 26μ, whilst the remaining length which was coiled within the protoplasm of the cell was 13μ long.

Special attention was directed to the red cells in the early stages, and every attempt was made to try to find any bodies within their interior of the nature of piroplasms. In not a few red cells specks of stained substance were found, lying for the most part towards the margin of the corpuscle. These, when examined with the highest power available (about × 3000), were seen to consist of small round-shaped dots often connected together by a very fine filament. They stain with Giemsa a dark dirty red colour, and not a distinct red as chromatin generally does. My friend Mr. E. M. Nelson kindly examined some films and recognised these intra-corpuscular bodies, but naturally was not able to express any opinion on their nature. He

very kindly took some micro-photographs of these structures at a direct magnification of 3000 diameters. I cannot lay much stress on the importance of such minute structures, but the fact that they were visible in the corpuscles in air-dried films before being subjected to any staining excludes the possibility of their being of the nature of a deposit or precipitate of stain on the surface of the corpuscle. I should add that they were most easily detected in dry unstained films when examined by dark-ground illumination, but this fact does not preclude the possibility of their being degeneration changes in the red cell.

Very prolonged and repeated examinations extending over several weeks were made of the numerous films of blood taken at all stages of this attack of blackwater fever, and as a result I would state that no form of malarial parasites or pigmented leucocytes was ever seen in the fresh preparations or in about 40 stained films most carefully and exhaustively examined.

Repeated examination of fresh cover-glass preparations both with ordinary and with dark-ground illumination failed to show anything moving in the plasma of the nature of a trypanosome or spirochæta. Stained films gave the same negative result.

Granular blue bodies with red-stained structures.—In some of the blood films taken towards the latter stages of the disease a few peculiar granular bodies were found. The earliest period at which one of these was seen was the fourth day of fever, and then only a single example was found, but they were more frequent on the last day. These bodies were only found after a careful search and were always exceedingly rare. In nine films only 36 such structures were detected, giving an average of 4 per film, which was about $\frac{1}{4}$ in. square. In some preparations only one granular body was found, whilst in another film as many as 17 were noted. They were not found in any of the films taken during the first four days.

In shape these bodies are nearly always spherical, sometimes oval, and very rarely somewhat irregular in outline. They have a very definite outline, and often a thick capsule or membrane seems to surround them. (See illustration.) The protoplasm stains usually a pale blue colour, sometimes a deeper blue, at other times a bluish-red tint.

These granular bodies varied in size. The average measurement of 30 specimens was 11.2μ in the longer and 10.7μ in the shorter diameter. The smallest typical example was round and measured 5μ ; the largest was oval and measured 17μ by 10μ in diameter. They do not contain a nucleus such as would be seen in a leucocyte, but contained within the protoplasm is a number of small round or oval dots which stain a deep chromatin red colour. These small structures are generally spread irregularly over the protoplasm of the cell, and are often more numerous in the centre than at the margins. The number of chromatin-stained bodies contained within one cell varies considerably, but probably there may be as few as 40 or as many as 200. In most specimens these chromatin dots are situated in a small unstained area, or each dot is surrounded by a narrow ring of faintly stained structure.

These minute intra-corpuscular bodies have a very vague outline, but when examined with the highest powers appear to consist of a dot of chromatin surrounded by a small amount of protoplasm. They appear round or oval and measure about 0.3μ to 0.75μ in diameter. Somewhat larger ones are seen oval or rod-shaped measuring 0.8μ by 0.4μ . Sometimes the chromatin dot has a tail of protoplasm and the whole body resembles that of a minute tadpole. Similar bodies are met with in the protoplasm of a few very large mononuclear leucocytes.

What is the nature of these granular blue bodies containing red-stained structures? The fact that they were only found towards the end of the disease when the blood was very rapidly becoming anæmic, and that they were then associated with the presence of nucleated red blood corpuscles, might suggest that they were degenerative red blood corpuscles containing nuclear remains or nuclear dust. Their general appearance, their staining reaction, the marked contour or outline, not to mention their size, seemed to negative this theory.

The second possibility is that they might represent some form of leucocyte, such as mast-myelocyte or myeloblasts of Ehrlich and Naegeli. Against this view is the fact that they possess no nucleus; that they do not in the slightest degree

resemble any of the coloured plates given by Ehrlich and Lazarus of the pathological forms of leucocytes just mentioned; and that during a prolonged period—some 20 years—in which I have been engaged in examining blood from various pathological conditions, notably the various forms of leucocythæmia, pernicious anæmia, aplastic anæmia, &c., I have never met any structures that have the slightest resemblance to these bodies.

Assuming, therefore, that these peculiar bodies do not represent any altered form of the cellular elements of the body, are they of the nature of protozoa? Are they related at all to those structures known as Koch's blue bodies, or do they belong to that vague family of cell inclusions, the chlamydozoa? Koch's granules, blue bodies, or Koch's plasma kugeln are circular, oval, or somewhat irregularly shaped cells which stain by Giemsa a blue colour and are filled with coarse chromatin granules. They have been proved by Gonder to represent certain stages in the life cycle of *Theileria parva*, the parasite of East Coast fever in

Blue-stained granular bodies with red-stained structures in their interior. From a blood film preparation fixed with osmic vapour and absolute alcohol, and stained with Giemsa. Drawn with Zeiss' camera lucida. Note the variation in size and the different number of red-stained structures contained within each. A granular body bursting and discharging its contents is seen at the lower left margin. A leucocyte and red blood corpuscle are drawn to show relative sizes of the granular bodies.

cattle. Gonder states that on an average the agamonts measure about 10 to 12μ , rarely 12 to 15μ . These structures are found in the internal organs of animals suffering from East Coast fever and a disease affecting calves in Uganda called by the natives Amakebe. They are seen in the spleen, lymphatic glands, bone marrow, and liver, but shortly before death they may sometimes be found in the circulating blood.

I find that the granular bodies that I have met with in the blood of this case of blackwater fever have some resemblance to Koch's bodies, but the chromatin granules in the latter are larger, more distinctly seen, and almost always more circular than the somewhat similar bodies I have described.

Against the theory of the relationship of the granular bodies to Koch's blue bodies is the fact that they were not associated with the presence of any definite piroplasms, unless the exceedingly small and ill-defined bodies which I have described in some of the red cells be regarded as of this

nature. On the other hand, it is possible that these peculiar bodies are of the nature of the chlamydozoa of Prowazek, a class of vague "organisms believed to be the cause of certain diseases of man and animals."

In conclusion, I would point out that possibly the peculiar granular bodies found in such small numbers in the circulating blood may be present in large numbers in the internal organs of cases of blackwater fever, and that they only reach the peripheral blood at the end of life. I would, therefore, suggest that those observers who come in contact with numerous cases of blackwater fever should examine smear preparations obtained during life by puncturing and aspirating a lymphatic gland, and in fatal cases have smears made from the spleen, bone marrow, lymphatic glands, and liver, to see whether analogous bodies can be found.

Bournemouth.

Medical Societies.

ROYAL SOCIETY OF MEDICINE.

SPECIAL MEETING OF FELLOWS.

*Continued Discussion on Alimentary Toxæmia.*¹

A MEETING of the Fellows of the society was held on April 28th, Sir FRANCIS H. CHAMPNEYS, the President, being in the chair.

Dr. WILLIAM HUNTER, re-opening the discussion, said that the subject matters of the discussion practically covered the whole series of processes which had been the special subject of his interest and investigations during the past 30 years. In the course of his studies relating to the nature of "pernicious anæmia" he had practically spent the greater part of his time in exploring in all their depths the muddy waters of the intestinal processes now brought under review. As the first and most important outcome he was enabled after three years experimental and pathological work to trace back this great anæmic disease to destructive (hæmolytic) changes affecting the blood in the portal system, induced by some special hæmolytic poison reaching it from the intestinal tract. These studies had founded and formed the basis of what had come to be termed "the doctrine of the enterogenous origin of severe anæmias," or "the toxic hypothesis" of the origin of these anæmias associated with his name and work. But although termed a "doctrine" or "hypothesis" his own work was an actual interpretation of the facts which he had ascertained experimentally—viz., that the blood changes of the disease he was studying could only be produced by special poisons which he employed. Further investigations as to the site of the lesions and the source of the infection which produced these particular hæmolytic toxins led him eventually step by step from the intestine to the stomach and finally to the tongue and to the discovery in these three organs of the infective lesions which always underlay this grave and mysterious disease. But they had also led him for the first time to recognise the far-reaching importance of the glaring septic lesions in the mouth—termed by him "oral sepsis"—as the greatest cause of infective disease in the body, and the chief cause of most of the disturbances in the alimentary tract, generally classed as toxæmic. Whatever rôle toxæmia—apart from lesions of the gastro-intestinal mucosa—played, either in health or disease, from an etiological, pathological, clinical, and practical point of view it was much more important to recognise that definite infective lesions, which were easily recognisable and in many cases could be easily dealt with, underlay nine-tenths of the disturbances of the alimentary tract which were termed "toxæmic." Dr. Hunter proposed, as his chief contribution to the day's discussion, to show by means of the epidiascope all sorts and sizes of oral streptococcal sepsis, which he would designate "the shark of the intestinal tract," and the multiple effects which it produced not only in that tract but elsewhere. He hoped he would thereby

make it clear that to describe such gross and obviously septic lesions of the mouth as he then showed under the euphemistic and belittling title of "toxæmia" was as illuminating and as helpful as if one applied the term "toxæmic" to a foul septic knife or sponge. The sharpest and broadest distinctions existed and should be drawn between processes in the mouth and processes in the gastro-intestinal tract in relation to the subject of "intestinal toxæmia or auto-intoxication." The mouth processes were not toxic in their character; if they had been so Nature would have provided for it by connecting up the mouth with the portal circulation. The toxicity of the gastro-intestinal processes, on the other hand, was a great physiological fact. The portal blood was always toxic even in health; the liver was the great antitoxic and excretory organ of the portal circulation just as the kidney was the great excretory organ of the general circulation. This toxicity was not an accident, nor did it depend on any one product of gastric or intestinal digestion. All attempts to connect it with any such product had, in his opinion, been futile. Far more conclusive evidence of the natural toxicity of the portal blood was presented every day in the facts of disease—in the disturbances connected with inefficient activity or actual disease of the liver. The most common evidences of portal toxicity were, in his judgment, those presented daily in surgical practice in the phenomena of the sickness, vomiting, headache, and sense of illness following the administration of anæsthetics, more particularly after prolonged administration. These were not due to the poisonous action of the anæsthetic *per se* on the nervous system, nor yet to the presence of food in the stomach or intestine; they were the direct result of the depressed activity of the liver cells induced by the anæsthetic and the consequent imperfect detoxication of the portal blood passing through the liver. If the energy of the liver cell (already depressed by disease and intensely aggravated by the unsound clinical practice of withholding food unduly from the patient prior to operation) completely failed, it became in consequence the victim of its own digestive ferments and its own self-digestion with resulting acute fatty degeneration and acute necrosis. The portal blood passed unchanged into the general systemic blood, producing the fulminating toxic disturbances of continuous sickness, vomiting, hæmatemesis, delirium, and coma, which characterised post-chloroform poisoning. Precisely the same phenomena producible experimentally (in Eck's fistula) by connecting up the portal vein directly with the inferior vena cava. He divided the causes of portal toxicity in health and disease into two classes—(1) non-infective causes, the various products of digestion formed by the ferments of the gastric, pancreatic, and intestinal digestion; and (2) infective causes, the various products formed by the action of bacteria on the food products, which were far more important as a cause of natural portal toxæmia. In health the chief and most abundant were those of the coli group. The degree of putrefaction varied according to the amount of proteid in the food, on the one side, and according to the abundance of coli on the other. The provision made by nature for due regulation of the latter was: first, the daily removal of the mass of excrement, alike of food and of organism in the fæces; and secondly, the provision of protective mucus which lined the whole gastro-intestinal tract, and of protective muscular movements which kept the whole gastro-intestinal contents in more or less continuous movement. In short, they were being continuously "moved on." Chronic constipation was therefore a highly unnatural condition and always a source of increased portal toxæmia. That it might exist in certain individuals as an almost permanent condition without apparently causing ill-health was solely due to the power and protective action of the liver. It was not any evidence of the comparative harmlessness of constipation *per se*, but only an evidence that some individuals possessed the cæcum and colon of an ox with the liver of a pig, capable of doing any amount of detoxication. The influence of the lactic acid group of organism in modifying the character and lessening the degree of putrefactive changes in the intestine was great and important. It had been investigated by him both by experiment and by clinical studies some 25 years ago, and recorded by him before the Royal Society (1890). The lactic acid group were the least harmful and most

¹ THE LANCET, March 15th (p. 754), April 19th (p. 1033), April 26th (p. 1163), 1913.