Average Differences.

Carotid artery—torcular =CO₂ 4.01 per cent.; O 4.76 per cent.
 —femoral vein=CO₂ 8.11 per cent.; O 11.91 per cent.

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REPORT ON

THE EFFECTS OF REPEATED HÆMORRHAGES ON THE COMPOSITION OF THE BLOOD.

By ARTHUR H. WHITE, L.R.C.P. & S.I.

(From the Pathological Department, University College, London.)

THE quantity of blood withdrawn was in each instance carefully estimated, and analyses of the various constituents were made, and then twenty-four hours afterwards a further careful bleeding and series of analyses and so on. The number of the successive bleedings in the case of the individual dogs varied from two to four. The analyses comprised the amount of water and solids, total proteids, fibrin, ash and ether extract, while in addition estimations were made of the corpuscular elements, the quantity of hæmoglobin, the specific gravity, and the coagulability. Investigations were made of the nature and character of the blood corpuscles, and also in one or two instances the histological changes in the glands, marrow, spleen, liver, etc., were partially examined.

Naturally in a research of this kind necessitating the immediate and simultaneous estimations of so many different things, some of the methods employed were not of the most exact nature, though sufficiently exact to give an approximate idea of the alteration; mostly, however, the method of analysis was as precise as possible—this being especially true in the cases of the water and solids, specific gravity, total proteids, fibrin, and ether extract.

The various points which I reported last year in regard to the disturbance in the relationship of the water and solids, the reduction in the specific gravity and in the proteids, the progressive increase in the fibrin, etc., have been amply confirmed by my later results, and are now ready for publication.

Below is a table giving the full results in the case of one of the dogs.

In addition to these results certain facts which bear on the question of blood regeneration have been elicited, and with regard to the regeneration or replacement of the red corpuscles, it would appear that in certain cases when the serum becomes too poor in solids there seems to occur at first an actual dissolution of many of the red corpuscles which had been left. This certainly appeared to have resulted in one case twenty-four hours after an excessively large quantity of blood had been taken away, as the reduction in the number of the corpuscles was far greater than was warranted by the amount of blood lost.

With regard to the histological changes in the organs resulting from these acute hæmorrhages I can as yet report no definite results. I may, however, mention that in two of the cases, one of which was the animal referred to above, the amount of blood pigment in the spleen and liver was larger than normal. There is, of course, always a marked decrease in the number of corpuscles, but this only affects the red, as there is almost always a marked leucocytosis.

For the examination of the blood on each occasion of bleeding from a dozen to a dozen and a-half coverslip preparations were prepared according to Ehrlich's method, and subsequently were stained with all the various stains recommended by Ehrlich and his pupils for the exhibition of the various classes of granules, but were singularly productive of negative results. Despite the increase in the white corpuscles I found that so far as the eosinophile granules are concerned the cells containing them were certainly not more than proportionately increased; this is quite in accordance with Ehrlich's statement that in acute leucocytosis the eosinophile cells are, if anything, lessened. The neutrophile granules I never found either in the normal or altered blood; Ehrlich himself states they do not occur in dogs' blood.

The increase in the number of leucocytes seems to be chiefly, if not altogether, due to an increase of the so-called polynuclear leucocytes, for in these cases they form, instead of the normal 75 per cent. or thereabouts, in some instances as much as 95 per cent. of the whole. Nucleated red corpuscles I never found unless in cases where the animals had been bled three or four times, and then only exceedingly rarely.

With regard to the hæmatoblastic crisis said to occur after hæmorrhage, I can say that in many instances there would appear to be an increase of the blood plates, in some few cases a marked increase. Whether such elements, however, previously existed in the circulating blood, or only appeared in the blood after withdrawal, is a matter of doubt.

REPORT ON

THE ACTION OF DRUGS ON THE LEUCOCYTES OF THE BLOOD.

By GEORGE WILKINSON, M.D.

(From the Pathological Laboratory of University College, Liverpool.)

I.—CHANGES IN THE NUMBER OF LEUCOCYTES.

DURING recent years several observers have recorded certain changes which take place in the number of the leucocytes of the blood of animals after the injection, either subcutaneously or directly into the circulation of bacteria, bacterial products, nuclei, peptone, and other substances. Acting on the suggestion of Professor Boyce, to whom I take this opportunity of expressing my thanks for much kind assistance, I have performed a series of experiments with a number of drugs, which were administered to rabbits by hypodermic injection, with the object of observing any changes that might occur, not only in the total number of leucocytes in the circulating blood, but also in the relative proportion of the mononuclear and polynuclear varieties.

	Blood Lost.		Weight of Dog in Kilos.	Specific Gravity.	In 100 parts of Blood.					Coagulation Time.	Hæmoglobin to Standard	Number of Red Corpuscles in 1 c.mm.	Proportion of White to Red.
	Grammes.	Percentage of Body Weight.			Solids.	Proteids.	Fibrin.	Ash.	Ether Extract.				
Normal blood	0.0	0.00	18.4	1052	17.85	15.04	0.37	0.81	0.13	—	94	5,730,000	1:690
Twenty-four hours after 1st bleeding ...	508.5	2.76	17.5	1048	17.06	14.53	0.41	0.81	—	45 to 50	66	4,490,000	1:457
" " " 2nd " ...	284.5	1.62	17.4	—	14.44	13.00	0.52	0.50	0.17	150 to 160	54	3,170,000	1:352
" " " 3rd " ...	252.0	1.44	17.2	1042	12.26	11.47	0.63	0.69	—	65	38	1,380,000	1:150
" " " 4th " ...	654.0	3.80	*	—	—	—	—	—	—	—	—	—	—

* On this occasion the animal was bled to death.

The following drugs have been used in the experiments: Potassium iodide, pilocarpin nitrate, atropine sulphate, digitalin, carbolic acid, turpentine, camphor, antipyrin, quinine hydrochlorate, salicin, and sodium salicylate. With each drug several experiments were made and various doses employed. Blood was obtained by pricking the animal's ear, and after dilution with Toison's solution the corpuscles were counted with the Thoma-Zeiss apparatus, every precaution being taken to avoid fallacy. The corpuscles were counted immediately before, and at various intervals after each injection; and at the same time cover-glass preparations of the blood were made and afterwards stained, usually with eosin and hæmatoxylin. From the latter the proportion of mononuclear to polynuclear forms was estimated by counting from 300 to 500 leucocytes.

The general results of the experiments may be stated thus: The first effect of the drug injection is to cause a diminution in the number of leucocytes per cubic millimetre. The degree and duration of the diminution varies with the drug employed, but with all those mentioned above, unless the dose was very small, its occurrence was recognised when the blood was examined sufficiently early. As a rule, it was not of long duration; but a notable exception occurred in the case of one of the experiments with quinine hydrochlorate. A large dose (0.7 gramme) of this drug caused the death of the animal two days after the injection; the blood was examined frequently between the time of injection and its death, and on every occasion the scantiness of the leucocytes was very striking. Coincidentally with the diminution in the total number of leucocytes, there was a distinct increase in the proportion of the mononuclear to the polynuclear varieties.

Following the diminution there was observed in the case of all the drugs employed an increase in the number of leucocytes per cubic millimetre. This change did not occur in the above-mentioned experiment, in which a very large dose of quinine was administered, but with smaller doses of this drug its occurrence was noted, although, as with salicin and salicylate of sodium also, the degree of increase was slight in comparison with that which followed the injection of the other drugs. With nearly all of them the increase was a much more evident phenomenon than the preceding diminution, and was of much longer duration. It was further constantly distinguished by the fact that the polynuclear leucocytes were relatively more increased in number than the mononuclear forms.

With atropine, and also with pilocarpin, a series of injections were made on one animal at intervals of twenty-four hours for several days. The leucocytes were counted immediately before, and at frequent intervals after, each injection. The first injection of each series was followed by a diminution in the leucocytes per cubic millimetre, which again was rapidly succeeded by a marked increase. The latter had not passed off at the end of twenty-four hours, when the next injection was given, but the sudden fall which followed each injection was very striking, as were also the coincident changes in the relative proportions of the mononuclear and polynuclear leucocytes. Indeed the alterations were so distinct that they could be recognised almost by a glance at the stained films, which were made at the same time, without counting at all. These changes in the number and relative proportions of the leucocytes are analogous to those which have been described by several observers as occurring after the introduction into the circulation of bacteria, bacterial products, etc. Sherrington has described similar changes in the blood of dogs and cats as the result of acute local inflammation.¹

II.—CHANGES IN THE STRUCTURE OF LEUCOCYTES.

I have also observed certain changes in the structure of the leucocytes under the influence of repeated doses of pilocarpin. Two grains of this drug was given hypodermically every twenty-four hours for seven days to one rabbit, and for fourteen days to another. Numerous cover-glass preparations of the blood were made at different times of each day, and they were stained in series by different methods, care being taken that all the specimens of a series were exposed to staining fluids of the same strength and for the same length of time. These specimens exhibit a remarkable change in the

structure and staining reactions of the small oxyphile leucocytes. The cells of this variety in the normal rabbit are full of very definite granules which stain readily with eosin and other acid dyes. Under the influence of the repeated doses of pilocarpin the granules become gradually less distinct, and eventually the protoplasm appears perfectly homogeneous and takes up the stain very feebly. In one of the animals this change was found to be very pronounced in so short a time as fifteen minutes after the first dose of the drug. The reaction of the nucleus of this variety of leucocyte to nuclear stains becomes diminished in a corresponding degree. On the other hand, the large oxyphile leucocytes with coarse granules (Ehrlich's eosinophile cells) show no change whatever, and stand out in marked contrast to those of the other variety. The red blood-corpuscles are also unchanged.

REPORT ON EXPERIMENTAL INVESTIGATIONS IN NEUROPATHOLOGY.

By J. S. RISIEN RUSSELL, M.D., M.R.C.P.,
Research Scholar to the British Medical Association.

I.—CEREBELLUM.

PHENOMENA resulting from the interruption of afferent and efferent tracts of the cerebellum have engaged my attention largely during the year. I had two objects in view in undertaking the researches; the first was to obtain evidence in support of or against the opinion that the cerebellum exercises a direct influence on the spinal centres, as opposed to any indirect influence exerted through the agency of the cerebral cortex; the second was to ascertain whether any descending tract could be traced from the cerebellum by way of which any such direct influence could be brought to bear on the spinal centres.

The results of the former of these investigations are embodied in a paper which has been presented to the Royal Society, while the results of the other part of the researches were brought before the Pathological Section of the British Medical Association at the annual meeting at Carlisle.

The best way to obtain the evidence sought for appeared to be by dividing the inferior cerebellar peduncle on one side, leaving the organ itself and its other peduncles otherwise intact. To perform this operation without injury to the auditory nuclei, and without including some fibres of the superior peduncle in the lesion, was no easy task, for it was, of course, necessary to divide the inferior peduncle close to the cerebellum, so as to include all the fibres leaving the organ by that peduncle.

The results of these experiments were controlled by others in which partial lateral section of the medulla on one side was performed in such a way as to interrupt the direct cerebellar and lateral medullary tracts without implicating the posterior columns and their nuclei on the one hand, or the olive and pyramid on the other. Further control experiments consisted in dividing the posterior columns and their nuclei on one side by a transverse incision made a few millimetres above the calamus scriptorius.

Animals on which these different operations were performed were allowed to live for various periods after the lesion was made, in order to compare the immediate effects of such lesions with the remote effects as observed some weeks later. The phenomena which resulted on section of the inferior cerebellar peduncle close to the organ, and those which resulted when the direct cerebellar and lateral medullary tracts were interrupted in the medulla oblongata, agreed closely; while the results of transverse section of the posterior columns and their nuclei differed widely from these. The remarkable provisions for compensation which exist in the central nervous system, and which become evident after lesions of different parts of that system, were strikingly seen in the cases of the animals on whom the above operations were performed; for whereas the most marked disorders of function resulted immediately after the operations, these were so far compensated for in the course of three to four weeks that it was difficult to believe that the same

¹ *Proc. Roy. Soc.*, vol. xv.