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.

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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.

animal so recently was the subject of such marked disorders of function.

Further experiments consisted in testing the electrical excitability of the two cerebral hemispheres: (a) after one inferior peduncle of the cerebellum was divided; and (b) when partial hemisection of the medulla oblongata was performed, in which all the structures on one side, with the exception of the pyramid, were divided.

In another series of experiments general convulsions were induced by the intravenous injection of absinthe under similar circumstances as in the last set of experiments, and also after transverse section of the posterior columns and their nuclei on one side.

Among the many important and interesting phenomena the outcome of the last two classes of experiments two facts stand out prominently: the electrical excitability of the opposite cerebral hemisphere is less than that of the hemisphere on the same side after section of the inferior peduncle of the cerebellum, and after partial hemisection of the medulla in which the pyramid was alone left intact; similar preliminary procedures result in exclusion of absinthe convulsions, otherwise general, from the muscles of the anterior extremity on the side of the lesion.

The central nervous systems of the animals on whom the section experiments were performed, and who were allowed to live for some weeks after the lesion was produced, were preserved, and subsequently submitted to careful microscopic examination, in which the Marchi method was employed to trace the tracts which degenerated in consequence of the different lesions. This portion of the research, though not yet quite complete, has supplied important information both as regards the supposed tract from the cerebellum to the antero-lateral region of the spinal cord, and as regards the existence of descending fibres other than those of the crossed pyramidal tracts of the cord, which, however, occupy a region of the cord close to these pyramidal fibres, both of which points are the subject of much controversy.

II.—THE CROSSED KNEE-JERK.

The "crossed knee-jerk" has also been the subject of an experimental investigation during the year, and the results of the investigation have been published in the *American Journal of the Medical Sciences* for March, 1896. A paper by two of Weir Mitchell's followers, published in the *International Medical Magazine* for June, 1895, was the means of re-directing my attention to the knee-jerk as a subject for further experimental investigation. This paper contained views and hypotheses with regard to the "crossed knee-jerk," and with regard to the subject of "reinforcement" of the knee-jerk, which it seemed important to submit to the test of experimentation, so contrary were they to the evidence supplied by previous experiments in this connection.

With regard to the "crossed knee-jerk," it is supposed that "the first effect of the tap on the patellar tendon is a centripetal impulse producing activity of a portion of one cortical motor area, this in turn stimulating the corresponding portion of the other hemisphere and producing thereby a contraction of the adductors of the thigh opposite to the one originally struck." If the phenomenon depends on an impulse passing from the "motor" cortex of one cerebral hemisphere to the other, the most likely path along which such an impulse will travel is the corpus callosum. I therefore divided this structure in the middle line in animals. Asphyxia was then induced in the animal by preventing air from entering the trachea, the result of which procedure was to cause an increased activity of the knee-jerks. Under these conditions it was possible to elicit beyond all question the so-called "crossed knee-jerk"—a result strongly opposed to the view put forward in the paper to which I have alluded.

I next determined to test whether the cerebrum took any part whatever in the production of the "crossed knee-jerk." I accordingly divided the spinal cord transversely in the mid-dorsal region so as to completely sever all connections between the cerebral centres and those of the lumbar cord on which the knee-jerk depends. In the course of a week after this operation it became possible not only to evoke a "crossed knee-jerk," but a greatly exaggerated crossed jerk, so that a tap on one patellar tendon not only evoked clonus in the extensors on that side, but also a powerful contraction of the

adductors of the opposite thigh, and even of the extensors of that knee.

Another effect observed which is of interest, was that sometimes a tap on the distal end of the femur or proximal end of the tibia resulted in both crossed phenomena, while there was no response in the extensors of the knee on the side on which the blow was delivered. That the "crossed knee-jerk" can be elicited at all, after complete section of the spinal cord above the lumbar enlargement, is proof that any explanation of its occurrence which supposes the necessity of an arc in which the brain is included does not fully meet the requirements of the case.

The view advanced with regard to "reinforcement" is that first advanced by Weir Mitchell; it supposes that "since the knee-jerk is reinforced by voluntary movement in any part of the body, that this reinforcement is due to an irradiation of motor impulse from the active centres to other similar centres, so that they and their related muscles acquire a heightened responsiveness to the external stimuli." There are many facts which can be advanced against this hypothesis; but experimentally I have satisfied myself that ablation of one cerebral hemisphere in an animal results in increased activity of the opposite knee-jerk, and that complete transverse section of the spinal cord at a level high enough not to interfere directly with the lumbar centres results in exaggeration of the knee-jerk in animals. Both these results support strongly the view which, in common with many neurologists, I hold with regard to "reinforcement," namely, that the spinal centres are normally under a certain amount of restraint or inhibition exerted on them by the cerebral centres, and that so-called reinforcement consists in a lessening of the inhibition.

III.—TORTICOLLIS.

There is an abundance of evidence to show that in spasmodic torticollis measures such as division of muscles, and stretching of the spinal accessory nerve, are useless, and that there must be few cases in which excision of a portion of the spinal accessory nerve can be expected to lead to permanently good results, in that in the majority of cases which come under observation muscles beyond the control of this nerve take part in the spasm. The only surgical measure which offers a reasonable prospect of permanent relief is division (with excision of portions) of the posterior branches of the upper cervical spinal nerve roots. This being the case, it seems of no small importance that we should accurately determine, by experiment: (a) The exact number of nerve roots, excitation of which, electrically, result in contraction of muscles which bring about movements of the head on the trunk; (b) The precise position in which the head is placed by contraction of the group of muscles supplied by each individual nerve root; (c) In how many roots a given muscle is represented; and (d) The muscles represented in each root.

This has been the subject of a third investigation during the year, the results of which I hope to publish as soon as possible, as the research is practically completed. The experiments have been conducted on monkeys in whom the upper spinal nerve roots have been exposed in the neural canal, and after section of the posterior roots and the roots of the spinal accessory nerve, the anterior roots, from the first cervical to the last thoracic, have been stimulated with the induced current.

In the first series of experiments the movements and position of the head were noted on excitation of each root; the muscles which bring about these movements were next exposed by dissection, and the exact muscles which contracted on excitation of any given root were directly observed in one series, while these results were controlled by observing each muscle in turn, and noting the precise number of roots, excitation of which resulted in contraction in the particular muscle under observation.

A NEW ISOLATION HOSPITAL.—The Rural District Council of Basford are just now completing their new isolation hospital, which is considered to be a good example of an up-to-date hospital. It will open for public inspection during the first fortnight in October, and Dr. Wray, the Medical Superintendent, will be happy to afford any information to any of his professional brethren who are about to get similar hospitals built by their councils.