Later examination of the blood showed haemoglobin 12 per cent., leucocytes 107,000, and red corpuscles 815,000 per c.mm. At the necropsy the ribs, manubrium sterni, and numerous other bones showed green material in the medulla. The periosteum of the vertebrae, from the neck to the pelvis, was infiltrated with the same green material, as was also the dura mater, the pericranium beneath the temporal muscle, the orbital cavities, the kidneys, the pancreas, and the glands just above the pancreas, the soft palate, tonsil, pharynx, mouth, and gums. The brain and spinal cord were healthy. Microscopically, the tumours consisted of large, round or oval-shaped cells, slightly larger than a white blood corpuscle, and containing often more than one nucleus, and occasionally a nucleolus. These cells were either embedded in an intercellular amorphous material of a very clear and transparent character or in a delicate network. At other times the tumour was interspersed with coarse bundles of connective tissue. In the midst of this granules with highly refractile properties were found lying in and between the cells.

I think it will be seen from this account that, with the exception of the involvement of the liver, this case very closely resembled my own, and would probably have still more closely resembled it had the life of my case been sufficiently prolonged.

A summary of the characteristics of the disease chloroma has been given by Hüber,¹⁵ by Dock,³ and by Byrom Bramwell.⁶ Hüber based his remarks on seven cases. His oldest patient was 24, and he found that males were more often affected than females.

There were usually general symptoms such as dullness, apathy, pallor, and palpitation of the heart. There was often exophthalmos with violent pains and frequently deafness. There was frequently epistaxis and difficulty of breathing from tumours in the nasal cavity. The brain and nerves were not often affected. Headache and giddiness, apathy and somnolence, were common. Purpura and haemorrhages were frequent, and the blood condition above described was characteristic. Körner describes tinnitus and deafness in ten cases,¹⁸ and Behring has seen apoplecticiform seizures.⁴ In Waldstein's case the urine was yellowish green.²⁷ Dock, who published his paper in 1893, based his analysis on 17 cases. His results in the main agree with Hüber's. The average age in 15 cases was 15.26 years. In Waldstein's case the age was 44. The average duration of the illness in 12 cases was 5 months. The early symptoms were pallor in 6 cases, emaciation 3, nose bleed 3, scorbutus 1, petechiae 1, loss of energy 2, fever 1, frequent pulse 3, headache 3, tinnitus aurium 2, deafness 7, double vision 1, loss of vision 2, exophthalmos 6, facial paralysis 2, feeling of oppression 1, prominence of temples, tumour of mammary region, feeling of constriction, toothache, 1 each.

The symptoms occurring later on were thirst, fatigue, strabismus, double vision (in addition to those mentioned above), deafness, otorrhea, pain in epigastrium, dyspnoea, abscesses, anaemia, oedema, haemorrhages from the lungs, intestines, in the skin and from the nose; obstruction of the nose, fever, frequent pulse, nephritis, irritability, coma, delirium, convulsions, wasting, constipation, vomiting, involuntary stools, diarrhoea, anorexia, pain in the region of the liver, craving for meat (King and Dock), disgust for meat (Aran), enlargement of spleen (2, probably 4 cases), swelling of thyroid. Death occurred from profound exhaustion, inability to take food, and often with some of the nervous symptoms mentioned above.

It will be seen from Dock's account that he has put down all the symptoms that occurred in all the cases. Many of them are of course in no sense characteristic of the disease and are, indeed, often mutually contradictory. Byrom Bramwell's summary, which is more recent, is perhaps more helpful in enabling us to attain a clear idea of the characteristics of the disease. He finds that in typical cases the characteristic features are as follows:—

1. The presence of lymphoid deposits in the orbits, temporal fossae, and periosteum of the bones of the skull, and the symptoms and signs arising therefrom.
2. The green colour of the lesions.
3. A profound blood change, of which the characteristic feature seems to be an enormous excess of lymphocytes.
4. The bone marrow, spleen, lymphatic glands, and organs throughout the body are affected (infiltrated with lymphoid deposits) as in lymphatic leukaemia.

Finally, may I be allowed a last word about the nature of the disease? Virchow regarded it as a kind of sarcoma. Byrom Bramwell seems to regard it as possibly identical with lymphatic leukaemia: I suppose a lymphatic leukaemia with local deposits. Dock does not seem to regard it as a sarcoma because of the absence of polynuclear giant cells.

On the other hand, the erosion of the bones which occurs

in some cases, and which was present in the calvarium of my case, is certainly suggestive of sarcoma.

May it not be possible that both views are right? That lymphatic leukaemia is, as it were, a fluid sarcoma of the haemopoietic system, and that chloroma is only another manifestation of the same disease characterized by solid deposits.

REFERENCES.

- 1 S. Ayres, *Journ. Amer. Med. Assoc.*, Chicago, 1896, xxvii, 986-988.
- 2 Aran, *Arch. Gén. de Méd.*, 1854, T. ii, P. 385.
- 3 Balfour, *Edin. Med. and Surg. Journ.*, 1835, xliii, p. 319.
- 4 Behring and Wicheskievicz, *Berl. klin. Woch.*, 1882, S. 509.
- 5 A. Burns, *Observ. on the Surg. Anat. of the Head and Neck*, 1st Amer. Edit., Baltimore, 1823, p. 386.
- 6 Byrom Bramwell, *Lancet*, 1902, vol. i, p. 520.
- 7 Scottish Med. and Surg. Journ., 1902, vol. x, p. 219.
- 8 H. Chiari, *Zell. f. Heilk.*, 1883, Bd. iv, S. 177.
- 9 T. v. Dock, *Amer. Journ. Med. Sci.*, 1893, n. s., C. vi, 152-185.
- 10 Dressler, *Arch. pf. ath. Anat.*, etc., 1866.
- 11 G. H. M. Dunlop, *Lancet*, 1902, vol. i, p. 451.
- 12 Durand-Fardel, *Journ. Heb. d. Prog. d. Sci. Méd.*, 1836, T. iii, p. 207.
- 13 F. G. Gade, *Nord. Med. Archiv*, 1884, xvi, No. 19, 1-24.
- 14 T. Harris and F. C. Moore, *Lancet*, 1902, vol. i, p. 525.
- 15 Höring, *Ein Beitr. z. Kent. d. Chloroma*, Brunswick, 1891; *Arch. d. Geb. d. Path. Anat. Inst. zu Tübingen*, Brunswick, 1891, vol. i, 180-93.
- 16 Huber, *Arch. d. Heilk.*, Bd. xix, S. 128, Leipzig.
- 17 R. Hutchison, *Med. Annual*, 1903, p. 187.
- 18 King, *Month. Journ. Med. Sc.*, 1853, vol. xvii, p. 97-104.
- 19 Körner, *Arch. Otol.*, New York, 1897, vol. xxvi, p. 289-93.
- 20 G. Lang, *Arch. Gén. d. Méd.*, Paris, 1893, vol. ii, p. 555, and 1894, vol. i, pp. 63, 186, 313.
- 21 Paviot and Gaillois, *ibid.*, 1896, vol. x, 570; *Compt. Rend. Soc. de Biol.*, Paris, 1896, vol. x, S. 3, 919-21; *Lyon Méd.*, 1896, C. xxxiii, 488-90, 1; *Mem. et Compt. Rend. Soc. de Sc. Méd. de Lyon*, 1897, C. xxxvii, pt. 2, 176-8.
- 22 V. Recklinghausen, *Tabegl. d. Versamm. Deut. Natur. u. Aerzte*, Strassburg, 1885, L. viii, 421.
- 23 W. Risel, *Deut. Arch. f. klin. Med.*, 1901, Bd. lxxii, p. 31.
- 24 W. Rosenblath, *ibid.*, 1901, Bd. lxxii, p. 1.
- 25 L. R. Sutherland, *Scot. Med. and Surg. Journ.*, 1902, vol. ii, p. 137.
- 26 E. Trevischick, *Lancet*, 1903, vol. ii, p. 183; *ibid.*, 1903, vol. ii, p. 530.
- 27 Waldstein, *Virchow's Archiv*, 1883, Bd. xci, S. 12.

ON THE RELATION OF THE ARGYLL-ROBERTSON PHENOMENON TO SYPHILIS.*

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THE object of the present paper is to offer some observations on the relation of the Argyll-Robertson phenomenon to a past syphilitic infection. It is hardly necessary to allude to the importance of this sign as a frequent and often early symptom of certain degenerative diseases of the central nervous system.

With regard to the general incidence of the symptom, it is now usually stated that it occurs in tabes dorsalis, general paralysis, and acquired or congenital syphilis, and that it is only exceptionally found in other diseases of the nervous system. Thus Dr. Mott¹ says that "practically speaking reflex rigidity of the pupils to light and pain exists only in tabes, general paralysis, and acquired or congenital syphilis;" he adds that very rarely cases of focal cerebral lesions, especially of the corpora quadrigemina, may show Argyll-Robertson pupils, and that "some authors point out that in alcoholism and other diseases reflex rigidity of the pupil may exist, but these are cases complicated by syphilis."

Dr. James Taylor² writes to the same effect, and says that "its frequent association with diseased conditions of the nervous system, usually regarded as syphilitic or parasymphilitic, and its occurrence as an isolated phenomenon in patients with a syphilitic history makes it possible that this disease has a close causal connexion with it."

Sir William Gowers,³ after remarking that it is chiefly seen in tabes and general paralysis, and occasionally in other degenerative diseases of less definite type, states that when he had found it existing alone, in most of the cases there had been constitutional syphilis many years before.

Drs. R. Cestan and Dupuy-Dutemps,⁴ in a paper on the Argyll-Robertson phenomenon, based on the examination of a large number of cases, state that, apart from tabes and general paralysis, it is altogether exceptional to find this sign either occurring as an isolated symptom or associated with other mental or organic nerve disease, and they conclude that its presence points to congenital or acquired syphilis, with a possible exception for some cases of syringomyelia and of the interstitial hypertrophic neuritis of Déjerine.

We should expect, therefore, to find, according to authors, reflex pupil rigidity most frequently, apart from tabes and general paralysis, in cases of former syphilitic infection.

Tabes and general paralysis are now very generally regarded as, in most cases, the remote consequence of a past attack of syphilis, as parasymphilitic affections. In a small number of cases, however, no history or evidence of syphilis

* Read at a meeting of Bath and Bristol Branch.

can be obtained, and although some of these may still be held to be syphilitic, the infection being purposely concealed or having escaped notice from taking place in an unusual way, yet in some of them it is possible that there is some other precursor, the nature of which is at present unknown. Nor is the exact process set up by syphilis known, but it may be conceived with great probability as a profound disturbance of nutrition slowly established as a consequence of syphilis, or as a kind of chronic blood poisoning from the same cause, leading to degeneration of certain parts of the central nervous system.

It is possible, however, that there is some other factor, at present unknown, which, working in conjunction with the syphilitic poison, leads to this chronic degeneration. Whatever the exact origin of the process, it is certain that it is of a different kind to the ordinary visceral (gummatous) lesions of syphilis, and that tabes and general paralysis stand on a totally different footing from the latter. If, therefore, the Argyll-Robertson phenomenon is part and parcel of the degenerative process of tabes or general paralysis, one would not regard it as likely that it should occur as a result of syphilis alone, but only when there is added to syphilis that special additional change which results from the infection, and is a further stage in its action in those patients who are to become victims of these diseases, and which induces the degeneration proper to them; this further stage itself being either the remote but direct consequence of syphilis, or, on the other hand, the result of the combination of syphilis with some other unknown factor.

It is of course a well-known fact that reflex pupil rigidity is sometimes found in patients without other signs of tabes or general paralysis being present, and with a history of past syphilitic infection, and the question arises as to the meaning of such cases. Two views are open with regard to them, on the one hand the Argyll-Robertson phenomenon may occur simply after syphilitic infection without further development of it, on the other its presence is evidence that the degenerative process underlying general paralysis or tabes is in existence. If the former is correct the presence of reflex pupil rigidity as an isolated symptom is of no particular moment, except that it may be of value as evidence of past syphilis; if the latter it must always be a serious symptom, for although in a few persons no further symptoms of these diseases may be developed, in which case we must conclude that for some reason the process has been checked, there is no guarantee in any particular patient that other symptoms may not occur at some future date, and in the majority it is an indication that degeneration is in active progress. The great frequency of reflex pupil rigidity in tabes and general paralysis, taking Mott's statistics¹ as 73.5 per cent in the former and 70 per cent in the latter, or including unilateral cases as 76.5 per cent. and 77 per cent. respectively, points strongly to the latter view as the correct one.

It seemed to me that if the Argyll-Robertson sign occurs in persons affected with syphilis but without any further (degenerative) change it should be most often found in cases in which there are gross syphilitic lesions of the brain or spinal cord. If, on the other hand, it should be absent or only exceptionally present in such cases it would be a strong argument that syphilis alone, even when the brunt of its incidence falls upon the central nervous system, is not sufficient to produce it, but that there must be in addition that further degenerative change which we have supposed to underlie tabes and general paralysis. I have, therefore, analysed, with a view of elucidating this point, the notes of cases of gross syphilitic disease of the nervous system; in all the cases there was an undoubted history of infection, with, in many the additional evidence of scars, skin lesions, ulcers, etc., in a few the diagnosis was confirmed *post mortem*, and in very many the effect of treatment must be considered as a further confirmation.

The cases were not selected except from the point of view of presenting certain evidence of syphilis; those in which there previously had been or was at the time of examination affection of the oculo-motor nerves were excluded as likely to cause confusion. My idea at starting, influenced by my reading, was that the Argyll-Robertson phenomenon would be found not infrequently in such cases, the result was therefore somewhat unexpected. The cases are 37 in number—31 males and 6 females; the average age was 36½ years, the average date of onset of cerebral or spinal symptoms was 13 years after infection. Twenty-eight were cases of cerebral syphilis; several showed slight optic neuritis; in 15 hemiplegia was the chief symptom; in 8 there were attacks of Jacksonian

epilepsy, in most unilateral, affecting one or both limbs on one side, and followed by paralysis of longer or shorter duration; in 5 other cases no definite paralysis was present, but characteristic headache, drowsiness, mental hebetude, epileptiform fits, etc. In one case the lesion was in the medulla oblongata, and in 5 the spinal cord was affected with meningo-myelitis.

Of these cases in 25 the pupils reacted well to light and accommodation; in 4, the reaction to light was feeble or sluggish but present, to accommodation normal; in 2, there was unilateral reflex pupil rigidity, but one of these must be deducted, as there was optic atrophy of old standing in the affected eye; in 4 cases the reaction to light was sluggish in one eye, but in two of these there had been paralysis of the third nerve on the same side, which had cleared up so far as regards oculo-motor paralysis, and in a third case there was some degree of optic atrophy with marked syphilitic changes in the retinal arteries. In all these patients reaction to accommodation was normal. Lastly, in 2 cases, in one of which slight optic neuritis was present, the pupils neither reacted to light or accommodation. So that in not one of these cases was the Argyll-Robertson phenomenon present in its complete form; in 2 it existed on one side, but one of these cases should probably be deducted for the reason given above; if, then, syphilis without further change is a cause of this sign it is somewhat remarkable that there was no typical example of it in the above series of cases of severe cerebro-spinal syphilis.

For purposes of comparison I examined my notes of the last 40 cases of tabes dorsalis that I have seen, and I found that reflex pupil rigidity was noted in 31, or 77 per cent. The number of cases with an undoubted history of syphilis was 26, or 65 per cent., and of these the sign was present in only 23, or 88 per cent. In addition there were 2 cases with the Argyll-Robertson phenomenon, who had had some venereal infection, which could not with absolute certainty be said to be syphilis. Further, reflex pupil rigidity occurred in 6 patients in both eyes, and in 1 unilaterally, who all positively denied syphilis. Such a denial does not obviously absolutely exclude syphilis, as they might have contracted it without being aware of it; but in order not in any way to beg the question I have taken these cases as non-syphilitic.

This number of cases of tabes was taken in order for better comparison with the cases of cerebro-spinal syphilis, and of course in such a small number I do not wish in any way to lay stress on the absolute percentages, but apart altogether from this the contrast as regards the occurrence of the Argyll-Robertson phenomenon between the two sets of cases is certainly very striking, and if the sign may safely be taken as one of degeneration within the central nervous system points to an essential difference between them.

If it is permissible to draw conclusions from this number of cases, the following would seem to be legitimate: That a previous syphilitic affection is not sufficient without some further change to lead to the presence of the Argyll-Robertson phenomenon, and in 37 cases of cerebral and spinal syphilis, where the mischief was confined to the ordinary visceral lesions of that disease, that is, gummata, gummatous meningitis, syphilitic endarteritis, the sign was not typically present. That in similar cases where it may be present, and in other cases with a history of past syphilis in which it occurs as an isolated sign of disease, it is evidence of a further degenerative process at work within the nervous system. That this degenerative process is to be regarded in the large majority of cases as a parasymphilitic one, although in a certain proportion proof of this is wanting, and there is possibly some other cause at present obscure. That this degeneration may remain stationary at an early stage without further development for long periods. If these observations are correct, the Argyll-Robertson phenomenon is an even more important sign of disease than it has been previously considered.

I may briefly mention that with regard to other affections of the pupils in these 37 cases of syphilis of the nervous system the pupils were both dilated in 7 cases, both contracted in 2, unequal in 18, and there was well-marked hippus in 1 case, in one eye in which a former third nerve paralysis had been recovered from.

REFERENCES.

- ¹ *Archives of Neurology*, vol. ii, p. 30.
- ² *Allchin's Manual of Medicine*, vol. iii, p. 388.
- ³ *Diseases of the Nervous System*, Second edition, vol. ii, p. 184.
- ⁴ *Gaz. des Hôp.*, 1901, p. 273.

BEQUEST.—Miss S. Peckover, of Wisbech St. Peter, has left £1,000 to the North Cambridgeshire Hospital.