Editorial.

NEUROSYPHILITIC UNCERTAINTIES.

It is probably the case that neurosyphilis is the outstanding disease of all those which have been associated with re-organised conceptions in the course of the last twenty or thirty years. A centuries-long era of mystery and empiricism came to an end with the discovery of the protozoal nature of the infection causing syphilis, the inevitable corollary being revision and re-systematisation of current views of its effects on the neuraxis and of the varieties of disease thereby produced. This wonderful spurt in the long race to the goal of perfected knowledge has been succeeded, however, by a period of 'marking time,' for the research that culminated in detection of the spirochaeta pallida has started almost as many problems as it has solved.

The spirochaete discovered by Schaudinn and Hoffmann fulfils all Koch's postulates; its morphology is thoroughly determined; it can be cultivated outside the body and kept going for many generations. But under ordinary conditions it seems to excite disease in man only, and to have no intermediary host. Whether it has a life-cycle in any way comparable to that of other protozoa remains at present indeterminate; in the primary sore and in the last stage of general paralysis its form is identical, as is also the case through many successions of artificial culture. Various modified shapes have been seen, but whether these are in process of degeneration or represent a resistive adaptation is not known.

When the spirochaete passes by perivascular lymphatics to become colonised at various points of the cerebrospinal vascular system local tissue-reactions ensue. It is doubtless possible for the organism to make its way from Virchow-Robin spaces into the interstices of the parenchyma, especially if the mesothelium is weakened by toxic influence, but in this particular variety of neurosyphilis it is mainly the mesodermal elements which react. The attack on the nervous system by invasion of the spinal fluid produces histological effects of a different character. Until certain questions connected with the functions and
interrelation of subarachnoid fluid-system and cerebral blood-system are satisfactorily elucidated a description of the exact way in which the brain parenchyma is reached must remain to some extent conjectural. Experimental, progressive, neurosyphilis has never as yet been characteristically produced. It is known that perineural lymphatics are open to injection from the subarachnoid space, so that invasion of the fluid therefrom can be accepted as a possibility; but whether perineuronic spaces are infiltrated from perivascular lymphatics or subarachnoid system is undetermined, and the experimental evidence is conflicting. On the whole, it is not, so far, proved that the fluid is the nutrient lymph of the brain, or that normally there is a flow from one system to the other via parenchymatous spaces. Nor must the fallacy of arguing from normal to diseased conditions be lost sight of. But this may be said, that if the spirochæte penetrates the brain from the vascular side it is difficult to see why the occurrence is not far more common; if from the meningeal and fluid side, its action in this respect is very different from that of many other organisms which, heavily infecting the fluid and meninges, are nevertheless scarcely ever found in the brain itself.

The formerly much discussed problem whether pathological distinctions of import can be drawn between vascular and parenchymatous neurosyphilis has now become largely meaningless. Wassermann reactions are positive in both types; the spirochæte is found with ease in many cases once classed as parasyphilis; a large part of the lesions of general paralysis is meningo-vascular; 'primary' optic atrophy is, in point of histological fact, also meningo-vascular; experimental pathology has succeeded in producing gummatous development in the testis of the rabbit by inoculation with material derived from the cortex of the paretic. It is no exaggeration to say that general paralysis is 'more syphilitic' than the varieties formerly classed as tertiary syphilis. Nor can clinical distinctions be maintained with the same absoluteness as in other days; in particular, the time-factor once confidently relied on is of no differentiating usefulness. Pathological evidence shows neurosyphilis to be one and indivisible. The existence of widely differing clinical types must of course be acknowledged, though on occasion they run into each other; their development depends largely on paths and sites of infection and on variation in local reaction. Old distinctions to some extent continue, but are oriented from a new standpoint. The question of why one
route should be taken rather than another is at present quite unsolved, and scarcely less obscure is the collateral problem of why, after latency sometimes measurable in decades, nervous symptoms should arise. It is possible the clue is to be sought in the theory of sensitisation by toxins, tissue resistance being gradually undermined by a process of 'hyperallergy,' so that in the end a minute toxic dose produces an exaggerated response.

Of several unsettled questions perhaps the most difficult relates to the problem of where, and in what form, the organism lies dormant until awakened into activity by alterations in immunity or nutrition, or, conceivably, by trauma. The interval between infection and the development of clinical manifestations is sometimes almost incredibly protracted. In some conjugal cases the presumption is that the seminal fluid is the carrier (the spirochaete is larger than the head of a spermatozoon); but what process of 'hibernation' the organism undergoes for these long periods is quite unknown.

A further undetermined question concerns the admittedly great disproportion between the incidence of syphilis and the appearance of the nervous variety—according to a commonly accepted view the latter is a sequel in only some three to five per cent. of infected subjects. Certain lines of evidence, both clinical and experimental, appear to lend support to a hypothesis guessed at by Fournier and in recent years often regarded with favour, to the effect that neurosyphilis is caused by a virus of neurotropic properties, a spirochaetal organism distinct from that responsible for syphilis with pronounced cutaneous manifestations, which is attributed to a dermotropic variety. Among the arguments for this contention are the observed facts that "mild syphilis is nervous syphilis" (Oskar Fischer), and that in numerous cases of juvenile tabes and general paralysis no cutaneous or mucous involvement has been seen. Nonne, too, has collected data showing that in the descendants of neurosyphilitic parents latency of primary and secondary symptoms is the rule. Reliance is often placed, further, on the experimental evidence of Levaditi and A. Marie, who obtained a dermotropic strain of organism from a testicular chancre in the guineapig (inoculated with human chancrous material), and a neurotropic strain from a similar guineapig chancre caused by infection with blood from a general paralytic; and who claimed to have demonstrated certain technical (cultural and other) differences between the two. But many serious objections may be raised to these lines of argument. Signs of
somatic syphilis are very common in cases of general paralysis (fibrosis of spleen, kidneys, liver, cerebral arteries); in that form of neurosyphilis syphilitic aortitis is often seen, exactly the same as that met with in somatic syphilis; the experiments mentioned above are vitiated by failure to exclude the possibility of the human chancrous material (from which the dermatotropic virus was derived) itself on occasion containing the neurotropic kind. Most significant of all is the invasion of the meninges and the presence of fluid reactions at the stage of ordinary cutaneous and mucosal secondary rashes. The argument based on the rarity of neurosyphilis in certain less civilised countries where syphilis is rampant is unimpressive, the facts being capable of another interpretation. Besides, cases are on record of the development of parenchymatous neurosyphilis in Europeans infected from such semicivilised sources. On the whole, firm proof of the dualist theory is still to seek.
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