SYPHILIS AS AN ETIOLOGICAL FACTOR IN MONGOLIAN IDIOCY.

BY D. O. RIDDEL AND R. M. STEWART, LONDON.

FROM time to time various theories have been advanced to explain the origin of Mongolian idiocy, but it cannot be said that the work of the last fifty years has much to justify a confident pronouncement on the etiology of this interesting and obscure disease. The condition seems to be essentially one in which hereditary influences play a subsidiary part, and consequently attention has been chiefly directed to the state of health of the parents and to a search for factors which might injuriously affect prenatal development. Down¹ himself considered tuberculosis in the parents an important etiological factor, but his conclusion has received little or no support from the observations of subsequent writers.

Stress has also been laid on the frequency of exhaustion of the reproductive functions in the mother, for the Mongol is often the last child of a mother nearing the menopause, but here again there are numerous exceptions which indicate that some other factor must be taken into account.

In appraising the value of any theory which is held to explain the origin of this disease, it is necessary to bear in mind that certain clinical conditions must be satisfied. First, although a history may be forthcoming of severe physical or mental shock to the mother during pregnancy, a Mongol may be born of a woman who was in apparent good health at the time of conception and during the whole period of pregnancy. Secondly, both parents may be at the zenith of their reproductive period of life, being neither unduly young nor unduly old. Thirdly, the Mongol may not only be the first and last born child, but may occupy an intermediate position in the family. Fourthly, pregnancies terminating in the birth of normal children may both precede and follow the birth of a Mongol, and lastly, the Mongol may be one of twins, the other being a perfectly healthy child. It follows, therefore, that general conditions such as uterine exhaustion, mental stress, and so on, cannot explain satisfactorily the origin of this disease, and, as Sutherland has pointed out, it is far more likely that such an exact type of disease owes its origin to one and the same cause in all cases. Although the physician is often assured that the health of the Mongol's mother was good throughout pregnancy, the possibility of some infection interfering with prenatal

development must always be entertained, and among those of an organismal nature syphilis, by reason of its prevalence and far-reaching results, demands first consideration. From this point of view it is instructive to recall certain of its peculiarities in relation to inheritance.

It is well known that the disease may be entirely latent, especially in pregnant women; there may be no rashes or other secondary manifestations, and a series of abortions may provide the first evidence of infection in the mother. It is also a familiar observation that there are numerous exceptions to the general rule which states that the degree of transmissibility of syphilis usually diminishes in proportion to the duration of the disease. While first pregnancies in infected women are usually likely to end in early abortions, followed in succession by late abortions, infected children and finally healthy offspring, it not infrequently happens that a syphilitic child is, as it were, slipped in between healthy children, much in the same way as the Mongol may occupy a place in the family between normal children.

Then again a syphilitic woman may give birth to twins one of whom presents stigmata of congenital syphilis, while the other enjoys immunity or shows no obvious symptoms.

It is clear that syphilis shows an extraordinary capriciousness in its transmissibility, and it seems to us no less clear that the explanation of Mongolism must be sought in some equally capricious factor. The question naturally arises, is it possible that the specific organism of syphilis is the cause of Mongolian idiocy? A review of the literature shows that there is no settled agreement on this question, and unfortunately few attempts appear to have been made to discover the frequency of syphilis in the parents of Mongolian children.

Sutherland ² appears to have been the first to suggest syphilis as an etiological factor, and out of his total of twenty-five cases there was evidence of syphilis in eleven instances, and in three others it was strongly suspected. In a series of twenty-six cases analysed by Muir ³ evidence of syphilis was obtained in three families. Comby, ⁴ in a review of seventy-nine cases, found evidence of syphilis in only ten patients. Goddard ⁵ states that of twenty-eight Mongols examined at the Columbus Institute, Ohio, 17·8 per cent. gave a positive Wassermann reaction.

On the other hand, Still ⁶ found evidence of syphilis in only one case in his series, and at the Killner Institute in Denmark the Wassermann reaction was negative in all cases. Van der Bogert ⁷ has recorded an extremely instructive example of the association of the two diseases in one family. Of four children the eldest was a typical Mongol with a positive Wassermann reaction in the blood. There had been no miscarriages and no history of syphilis could be obtained from the parents, but four years after the birth of the Mongol twins were born, one of whom (when examined at the age of five years) was a normal child with

a negative Wassermann reaction. The other was a congenital syphilitic bearing so close a resemblance to a Mongol that, when shown at a clinical meeting, he was accepted by all present as an example of this disease.

Babonneix and Blum⁸ have also reported two cases combining the features of Mongolism and congenital syphilis, and in an earlier contribution to the anatomical study of Mongolian idiocy Babonneix⁹ described the presence of a meningeal gumma in the sulcus separating the right prefrontal and postfrontal gyri. Another significant fact brought out by a review of the literature pertaining to Mongolism is the frequency with which the birth of a Mongol is foreshadowed by one or more miscarriages, and one of the most striking examples we have encountered relates to the history of an imbecile who is at present an inmate of the Leavesden Mental Hospital. The father, a commercial traveller, died of heart disease at the age of forty-two; he was described as a steady and industrious man, but never enjoyed good health. The mother stated that her health had always been excellent. During the first few years of married life she had six miscarriages—'small affairs'—followed by the birth of a succession of premature children. One was born dead at six and a half months; a second at seven months; a third, at seven and a half months, lived for one hour; a fourth, at eight months, lived three days; a fifth, at seven months, lived several hours. The sixth child survived, and is now nineteen years old, delicate, with a 'tendency to consumption.' The seventh child, a breech presentation case, showed the features of Mongolism, while the eighth and last child died at birth. At the time of birth of the Mongol the mother was in her fortieth year. A rough examination of her nervous system showed irregular eccentric pupils, reacting sluggishly to light, and absent knee jerks. Her blood Wassermann reaction was strongly positive; that of the Mongol was negative. Maternal histories as striking as the above are doubtless rare, but we have been able to discover numerous instances where a history of one or more miscarriages is mentioned. None the less, there are a large number of competent observers who state that syphilis cannot possibly be admitted as an etiological factor. Tredgold,¹⁰ for example, was unable to discover any predominance of syphilis in over twenty cases investigated by him, while Goddard⁵ states that he could find no conclusive proof that syphilis in the parent causes Mongolism, or indeed, feeble-mindedness of any type. He also considers that the lack of correlation between the incidence of Mongolism and this disease constitutes a fatal objection to the syphilitic theory. Mongolian imbecility is, relatively speaking, very rare; syphilis is far from rare; why, therefore, is this peculiar form of mental defect not vastly more prevalent than it is? The validity of an argument of this character seems to us to be decidedly open to question. It is well known that

certain congenital diseases, rarer even than Mongolism, may have a syphilitic origin, and if, for example, syphilis may produce infantilism, it is surely not illogical to suppose that under certain conditions, not as yet elucidated, it may also play a part in the genesis of Mongolian idiocy. It is a fact of common observation that conclusions regarding the incidence of syphilis based solely on historical data and clinical evidence are apt to be very wide of the mark, and to vary according to the preconceived idea of the investigator, and probably for this reason attempts have lately been made to settle the relationship of syphilis to Mongolism by the application of the Wassermann reaction. The number of cases examined, however, does not appear to be large, and we have been able to find only two papers dealing with the results in a reasonably adequate series of cases.

Stevens¹¹ applied the Wassermann reaction to the blood serum of thirty-eight Mongols and obtained positive results in 21 per cent., and in a second series¹² of eighteen, the test was positive in the blood in 33 per cent., and in the cerebrospinal fluid in 18·4 per cent. A novel feature of this investigation was the discovery that 97·4 per cent. of the spinal fluids gave a syphilitic curve with the colloidal gold reaction, and Stevens concludes that Mongolism is a result of syphilitic infection which probably 'acts primarily on some of the endocrine organs, possibly the pituitary.'

These results seem to go a long way towards establishing a syphilitic basis for the disease, but unfortunately the methods adopted by Stevens in interpreting the tests are open to criticism. The entire absence of pleocytosis noted by him is hard to reconcile with an increased globulin content in every case, and since no details are given of the technique employed in preparing the gold-sol it is possible that the syphilitic curves obtained were due to the use of an acid solution of colloidal gold. Furthermore, the degrees of precipitation noted by Stevens were in some cases extremely slight, no greater, indeed, than those which are occasionally found when normal spinal fluids are tested.

At a later date McClelland and Ruh¹³ repeated the tests on a different series of patients, thirteen in number, and obtained almost completely negative results. The Wassermann reaction was negative in all cases in both blood and cerebrospinal fluid; only two cases showed an increase of globulin by the Pandy test, and in every instance the colloidal gold reaction was negative. In view of the conflicting nature of these reports we have thought it desirable to examine a much larger series, and with the help of our colleagues at Caterham we have been able to apply these tests to fifty-five Mongols. The Wassermann reactions were carried out for the most part at Caterham Mental Hospital, and a few at Bethlem Royal Hospital, and we would like to place on record our thanks to Dr. Gordon and Dr. Lovell for their generous assistance. The spinal fluids

Case No.	Blood.	Cerebrospinal Fluid..												
	Wassermann Reaction.	Wassermann Reaction.	Cells per c.mm.	Globulin.	Colloidal Gold Test.									
					1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
1	—	—	1	—	1	1	2	2	1	0	0	0	0	0
2	—	—	1·3	—	1	1	2	2	2	1	1	0	0	0
3	—	—	1	—	1	1	2	3	2	1	1	0	0	0
4	—	—	0·6	—	1	1	2	2	2	1	1	0	0	0
5	—	—	1	—	1	1	2	2	2	1	0	0	0	0
6	—	—	3	—	1	1	2	2	2	1	0	0	0	0
7	+	—	1	—	1	1	2	3	2	1	0	0	0	0
8	—	—	1	—	1	1	2	2	2	1	0	0	0	0
9	—	—	2·3	—	1	1	2	2	1	0	0	0	0	0
10	—	—	2	—	1	1	2	2	1	0	0	0	0	0
11	—	—	2	—	1	2	3	1	1	0	0	0	0	0
12	—	—	2	—	1	1	2	2	2	1	0	0	0	0
13	—	—	1·3	—	1	2	3	3	2	1	0	0	0	0
14	—	—	4·6	—	1	2	3	3	3	1	0	0	0	0
15	—	—	2	—	1	2	3	1	0	0	0	0	0	0
16	—	—	1	—	1	2	3	2	1	0	0	0	0	0
17	—	—	1	—	1	2	3	3	1	0	0	0	0	0
18	—	—	1	—	1	2	3	1	1	0	0	0	0	0
19	—	—	1	—	1	1	3	2	2	1	0	0	0	0
20	—	—	1·6	—	1	2	3	3	1	0	0	0	0	0
21	—	—	0·6	—	1	2	3	3	2	1	0	0	0	0
22	—	—	1·3	—	1	1	2	3	3	2	0	0	0	0
23	—	—	1	—	1	1	2	2	1	0	0	0	0	0
24	—	—	0·6	—	1	1	2	2	2	1	0	0	0	0
25	—	—	0·6	—	1	1	2	2	2	1	0	0	0	0
26	—	—	0·3	—	1	1	2	2	2	0	0	0	0	0
27	—	—	1	—	1	1	2	2	1	0	0	0	0	0
28	—	—	0·6	—	1	2	2	1	1	0	0	0	0	0
29	—	—	0·3	—	1	1	2	2	1	0	0	0	0	0
30	—	—	0·3	—	1	2	2	1	1	0	0	0	0	0
31	—	—	2	—	1	2	2	1	1	0	0	0	0	0
32	—	—	3	—	1	1	2	2	1	0	0	0	0	0
33	—	—	1	—	1	2	2	1	1	0	0	0	0	0
34	—	—	0·3	—	1	1	2	2	1	0	0	0	0	0
35	—	—	1	—	1	2	2	1	1	0	0	0	0	0
36	—	—	0·6	—	1	1	2	2	1	0	0	0	0	0
37	—	—	0·6	—	1	2	3	3	2	1	0	0	0	0
38	—	—	1	—	1	1	2	2	1	0	0	0	0	0
39	—	—	0·3	—	1	1	2	1	1	0	0	0	0	0
40	—	—	2	—	1	1	2	2	1	0	0	0	0	0
41	—	—	0·3	—	1	1	2	2	2	0	0	0	0	0
42	—	—	1·3	—	1	1	2	2	2	1	0	0	0	0
43	—	—	0·3	—	1	2	3	2	1	0	0	0	0	0
44	—	—	1·6	—	1	1	2	2	1	0	0	0	0	0
45	—	—	1	—	1	1	2	2	1	0	0	0	0	0
46	—	—	0·3	—	1	2	2	1	1	0	0	0	0	0
47	—	—	3	—	1	2	2	1	1	0	0	0	0	0
48	—	—	0·3	—	1	1	2	1	1	0	0	0	0	0
49	—	—	2	—	1	2	2	1	0	0	0	0	0	0
50	—	—	0·3	—	1	2	2	1	1	0	0	0	0	0
51	—	—	1	—	1	2	2	1	1	0	0	0	0	0
52	—	—	2	—	1	2	2	2	1	0	0	0	0	0
53	—	—	1·3	—	1	1	2	1	1	0	0	0	0	0
54	—	—	0·3	—	1	1	2	2	2	1	0	0	0	0
55	—	—	3	—	1	1	2	2	1	0	0	0	0	0

were also examined for cell count and globulin content, and response to the colloidal gold reaction. In performing the latter we were careful to

use only neutral unprotected sols, prepared by the method of Miller, Brush, Hammers and Felton.¹⁴ Normal, syphilitic, and parietic fluids were used throughout as controls.

It will be seen from the accompanying table that the Wassermann reaction was positive only once in the blood, and uniformly negative in the spinal fluid. On the other hand, with the colloidal gold test, the precipitation curve characteristic of syphilis was found in nearly every fluid examined. The cell count and globulin content were within the limits of the normal in all cases.

The interpretation of these results is a matter of some difficulty, and at first glance it might be thought that the occurrence of only one positive Wassermann reaction in fifty-five samples of blood disposes of the syphilitic theory in a conclusive manner, but for several reasons it seems wiser to avoid such a conclusion. In the first place, the Wassermann reaction has the limitations which are attached to every laboratory test, and it by no means follows that a negative reaction excludes the possibility of infection. It would, of course, be absurd to disregard the significance of so many negative results, but the need for caution will be recognized when it is pointed out how often negative serological findings are encountered in congenital syphilis. In our experience the Wassermann reaction is far less reliable in congenital syphilis than in any of the acquired forms of the disease, for we have seen a large number of young adults presenting the Hutchinsonian facies whose blood and cerebrospinal fluid gave negative reactions, and such appears to be the experience of other workers. Wile and Marshall,¹⁵ for example, obtained a positive Wassermann reaction in only 16.9 per cent. of a series of fifty-three cases of congenital syphilis.

With regard to the precipitation curves obtained with the colloidal gold reaction it will be seen that while decoloration never proceeded very far, it was a constant phenomenon, and corresponded to the type of curve described by Eskuchen¹⁶ under the term 'lues latens.' It may be, as some writers have suggested, that this reaction is a more sensitive test for latent or inactive syphilis than the Wassermann test, but on the other hand it must be borne in mind that it is not specific, for the so-called luetic and parietic curves may be found in the spinal fluids of individuals suffering from non-syphilitic disease, such as disseminated sclerosis, lethargic encephalitis, diphtheria, and poliomyelitis, and it is possible that Mongolian idiocy must be added to the list. Furthermore, until the rationale of the test is more completely understood, arguments based on its behaviour are clearly inadmissible.

Thus far, our investigations have failed to substantiate the contention of Stevens that Mongolian idiocy is a form of congenital syphilis, but they do seem to confirm his conclusion that the cerebrospinal fluid of the Mongol has the property of precipitating solutions of colloidal

gold in the syphilitic zone. It may be that future investigation will show that under certain conditions a syphilitic infection of the mother may determine biochemical changes in the developing embryo which are ultimately expressed in the physical peculiarities of Mongolism, and we consider that at this juncture it would be unwise to conclude that syphilis plays no part in the origin of this disease. The subject is one calling for further elucidation, and it seems to us that investigation of the parents from this standpoint offers a fruitful line of inquiry.

REFERENCES.

- ¹ J. L. DOWN, *Clinical Lectures and Reports*, London Hospital, 1866, iii, 259.
- ² SUTHERLAND, *Practitioner*, 1899, lxiii, 632.
- ³ MUIR, *Arch. of Pediat.*, 1903, xx, 161.
- ⁴ COMBY, *Bull. soc. pédiat. de Paris*, 1922, iii, 85.
- ⁵ GODDARD, *Jour. Amer. Med. Assoc.*, 1917, lxviii, 1057.
- ⁶ STILL, *King's Coll. Hosp. Rep.*, 1898, vi.
- ⁷ VAN DER BOGERT, *Amer. Jour. Dis. Child.*, 1916, xi, 55.
- ⁸ BABONNEIX and BLUM, *Bull. soc. pédiat. de Paris*, 1922, iii, 85.
- ⁹ BABONNEIX, *Arch. de méd. des enf.*, 1909, 499.
- ¹⁰ TREDGOLD, *Mental Deficiency*, 1922, 240.
- ¹¹ STEVENS, *Jour. Amer. Med. Assoc.*, 1915, lxiv, 1636.
- ¹² STEVENS, *ibid.*, 1916, lxvi, 1373.
- ¹³ McCLELLAND and RUH, *Jour. Amer. Med. Assoc.*, 1917, lxviii, 777.
- ¹⁴ MILLER, BRUSH, HAMMERS and FELTON, *Johns Hop. Hosp. Bull.*, 1915, xxvi, 391.
- ¹⁵ WILE and MARSHALL, *Arch. of Derm. and Syph.*, 1921, iii, 273.
- ¹⁶ ESKUCHEN, *Die Lumbalpunktion*, 1919, 88.