A CASE OF THIRD GENERATION SYPHILIS*

BY

G. MASTERTON

Fife

The conditions of proof first suggested by Fournier (1891) remain, to this day, the acid test of third generation syphilis. With this in mind and allowing for current trends in congenital syphilis, transmission through three generations appears probable in the following family (Figure).

Since the serological findings were obviously of vital importance, the treponemal immobilization test (TPI) was used throughout the investigation.

* Received for publication April 3, 1956.

Case Reports

The clinical data are presented chronologically and not in order of original review. Unless otherwise stated, previous examination and treatment was at the local V.D. clinic. For clarity, the immediate members of the original patient’s family are reported separately, and laboratory findings are detailed in Table I.

IMMEDIATE FAMILY

Maternal Grandfather (I, 1) aged 70 years

1920. Commenced treatment for “latent syphilis”; 7 years previously complained of a genital sore followed by skin rash. Defaulted after only four injections of arsenic.

1955. 20 year’s history of progressively failing vision, and of gradual mental and moral deterioration. Is now morose, irritable, forgetful, and dirty. Clinically the classical picture of general paralysis of the insane emerges, with associated bilateral optic atrophy.

Maternal Grandmother (I, 2) aged 64 years

1920. Treated for “latent syphilis”. Her daughter (II, 5) had just developed acute congenital syphilis. Defaulted after 5 months’ treatment. Reappeared years

TABLE I

LABORATORY FINDINGS, 1955

<table>
<thead>
<tr>
<th>Patient</th>
<th>Serological Findings</th>
<th>C.S.F. Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Kahn</td>
<td>PPR</td>
</tr>
<tr>
<td>Gen. Case</td>
<td>Relationship to Original Patient</td>
<td>Recent</td>
</tr>
<tr>
<td>I 1</td>
<td>Grandfather .</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Grandmother .</td>
</tr>
<tr>
<td>II 3</td>
<td>Mother .</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>Father .</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III 2</td>
<td>Original Patient .</td>
<td>Positive</td>
</tr>
<tr>
<td>18</td>
<td>Husband .</td>
<td>Negative</td>
</tr>
<tr>
<td>1</td>
<td>Elder Sister .</td>
<td>Negative</td>
</tr>
<tr>
<td>3</td>
<td>Younger Sister .</td>
<td>Negative</td>
</tr>
<tr>
<td>4</td>
<td>Brother .</td>
<td>Negative</td>
</tr>
<tr>
<td>IV 2</td>
<td>Son .</td>
<td>Negative</td>
</tr>
</tbody>
</table>

† Grandfather's C.S.F. report "Cells 18/c.mm: Protein 80 mg. per cent.: W.R. + + : Lange gold curve 5554433210.
later but defaulted immediately. Serological findings: 1920, Wassermann reaction ++; 1921, Wassermann reaction ++; 1931, Wassermann reaction negative.

1955. 10 months' history of breathlessness and precordial pain on moderate exertion. Examination revealed a systolic murmur and accentuation of the second sound in the aortic area but no cardiac enlargement. Blood pressure 158/78. X-ray—"Dilatation of ascending aorta with calcification of the walls". Electrocardiogram—"Changes compatible with coronary ischaemia". Obstetric history (Table II).

**Generation II**

**Mother (II, 3) aged 40**

1915. Skin rash and snuffles at age of 4 months. Condition subsided without treatment. Was underweight and difficult to rear.

1920. Examined at clinic with sister (II, 5). Blood Wassermann reaction strongly positive. No treatment owing to default.

**1928. Typical attack of interstitial keratitis (bilateral) treated with eyedrops only. Condition recurred 9 months later but ultimately subsided.**

1955. Asymptomatic since 1928. Has typical congenital facies with bilateral corneal scarring and opacities. Given two courses of penicillin (16 mega units oily procaine penicillin). Blood Wassermann reaction titre one year after this treatment remains at the pre-treatment level.

**Father (II, 11) aged 42**


**Generation III**

**Children of II, 3 and 11 (III, 1 to 4)**

(1) b. 1933 F. No stigmata, age 22 yrs. Negative serological tests. Baby (IV, 1) born April, 1955, was clinically and serologically negative.

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### Table II

<table>
<thead>
<tr>
<th>Child</th>
<th>Year of Birth</th>
<th>Sex</th>
<th>Previous History</th>
<th>Present Condition</th>
<th>Remarks</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Age at Onset</td>
<td>Clinical</td>
<td>Serological</td>
</tr>
<tr>
<td>1</td>
<td>1913</td>
<td>M</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>1914</td>
<td>M</td>
<td>3/12</td>
<td>Hydrocephalus</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>1915</td>
<td>F</td>
<td>4/12</td>
<td>Snuffles</td>
<td>W.R.++</td>
</tr>
<tr>
<td>4</td>
<td>1917</td>
<td>F</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>1919</td>
<td>F</td>
<td>6/12</td>
<td>Snuffles</td>
<td>W.R.++</td>
</tr>
</tbody>
</table>

→ 1920-21. Mother treated for 5-month period. 4-45 g. arsenic given—Defaulted.

| 7     | 1924          | F   | —                | —                 | —         | —   | —   |
| 8     | 1926          | M   | —                | —                 | —         | —   | —   |
| 9     | 1930          | F   | —                | —                 | —         | —   | —   |
| 10    | 1931          | M   | —                | —                 | —         | —   | —   |


Regular blood donor.
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(2) b. 1935 F. Proband.
(3) b. 1942 F. Clinically and serologically negative, age 12 yrs.
(4) b. 1946 M. Clinically and serologically negative, age 9 yrs.

Original Patient (III, 2) aged 19 (Proband)
Uneventful infancy and childhood.
1946. Age 11 yrs. Bilateral “mistiness of vision” for several months. No actual inflammation seen. Treated with eyedrops only.
1954. When 4 months pregnant, referred to Venereal Disease clinic because of persistently positive blood Wassermann reaction. No previous venereal disease or extramarital exposure. No clinical evidence of acquired or congenital syphilis; cubitus valgus was the only abnormality noted. Eyes macroscopically normal. Later slit-lamp microscopy showed “Ghost vessels and deep corneal opacities characteristic of interstitial keratitis (I.K.).” As her husband was overseas, and not available for examination acquired syphilis could not be excluded. Intensive penicillin (16 mega units aqueous procaine penicillin) given immediately. Repeated at 36th week gestation. Blood Wassermann reaction titre was unaffected and 1 year later still remains at the pre-treatment level.

Husband (III, 18) aged 20
Regular soldier. No history or clinical evidence of previous venereal disease. Donated blood twice during 1954, and blood Wassermann reaction was then negative. X-ray of buttocks showed no evidence of previous bismuth injections.

Son (IV, 2), born March, 1955
Full-term healthy baby. Clinically and serologically negative at birth, 4 months, 9 months, and one year.

Son (IV, 3), born June 2, 1956
Healthy baby, birth weight 9 lb. 11 oz. Blood Wassermann reaction (heel stab) negative. No antisyphilitic treatment was given to mother, and her blood Wassermann reaction titre remains negative.

Other Relatives

Generation II
This generation falls conveniently into two groups: Those (infected) children born before their mother was treated in 1920, and those born thereafter (Table II). It seems that the very inadequate treatment she received has sufficed to protect the latter group.

Generation III
Sixteen members of this generation showed no clinical or serological evidence of syphilis. Of the two remaining the original patient (III, 2) has already been described; a brief note on her cousin (III, 6) follows:

Cousin (III, 6) aged 12
1955. Slit-lamp examination showed “healed subepithelial corneal opacities but no ocular evidence of congenital syphilis”. In the main, the serological findings were negative—although one laboratory reported “Wasserman reaction + : Kahn test +”: TPI tests where negative.

Discussion
Obviously some type of syphilitic infection is present in all three adult generations of this family—it remains to interpret these findings in the light of the Fournier–Finger philosophy (the Fournier criteria modified by the later influence of Finger, 1900).

Thus, third generation syphilis is probable only if:
(1) Congenital syphilis is
   (a) present in the second generation mother and her child,
   (b) present from early infancy.
(2) Acquired syphilis is
   (a) present in one or both grandparents,
   (b) absent in the second generation mother and her child,
   (c) absent in the second and third generation husbands.

1 (a). The mother (II, 3) shows definite signs of congenital syphilis. Despite the absence of a “typical” history, her daughter (III, 2) showed unquestionable evidence of previous interstitial keratitis. This, together with apparent sero-resistance after intensive treatment, makes congenital syphilis extremely probable. In contrast, her cousin (III, 6), whose history strongly suggested interstitial keratitis, was proved, on ophthalmic and serological grounds, not to be suffering from congenital syphilis.

1 (b). The absence of early infantile symptoms in the patient (III, 2) is not surprising if it be remembered that, by the time she was born, this type of congenital syphilis was already uncommon in Great Britain (Nabarro, 1954). Indeed, the contrast between the infancy of the mother (born 1915) and that of her daughter (born 1935) exemplifies the current trend of the disease in this country.

2 (a). Both grandparents are almost certainly suffering from the later effects of partially treated acquired syphilis. The grandmother’s doubtful TPI test in no way detracts from this view (Wilkinson, 1954). In many ways, it is a remarkable finding.
nearly a quarter of a century after the usual serological tests had become negative.

2 (b). On rare occasions, congenitally-syphilitic patients can be re-infected with the acquired form of the disease—which then follows its normal course uninfluenced by the pre-existing condition of the patient. Such an infection seems unlikely in either patient (II, 3) or patient (III, 2) for the following reasons:

(i) No evidence of acquired syphilis,
(ii) Husband not infected,
(iii) Blood Wassermann reaction titre unaltered by intensive treatment.

An alternative possibility in the daughter (III, 2)—asexually acquired syphilis—was similarly rejected, partly for the reasons given above and partly because none of her close domestic contacts appear to have suffered from contagious syphilis during her lifetime. It is obviously impossible to exclude any casual contact.

2 (c). Recent work (Sequeira and Wilkinson, 1955) indicates that the margin of error in suspected latent syphilis can be appreciably reduced by the TPI test. As a crucial point of the whole investigation was the exclusion of this form of syphilis from both husbands, great reliance was placed upon this test. The negative TPI results, whilst not infallible, at least make a previous untreated syphilitic infection very unlikely.

The evidence thus collected seems to satisfy the main Fournier–Finger conditions of proof. Although the original patient showed no evidence of infantile congenital syphilis, it seems unreasonable to attach too much importance to this omission. After all, this form of disease has been rare in Great Britain for the past 30 years.

In conclusion, although absolute proof is lacking, it does seem very probable that the original patient is indeed suffering from third generation syphilis.

Summary

1) Four generations were included in this investigation. Ultimately all but one of the 36 surviving members of the family were traced and examined.

2) An analysis of the collected evidence suggests that the main Fournier–Finger requirements have been satisfied. The one exception—absence of infantile congenital syphilis in the original patient—is in accordance with current trends of the disease.

3) The syphilitic infection present in the original patient (III, 2) is thought to be a true example of third generation transmission. She is the second child of a hitherto untreated congenitally-syphilitic mother.

4) The Treponemal Immobilization Test seems of particular value in such an investigation which is primarily concerned with long-standing, previously treated, or latent infections.

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