The question whether third-generation syphilis does occur has in the past been the subject of much debate and controversy. The following criteria laid down by Fournier (1891) and Finger (1900) still provide the yardstick by which third-generation syphilis is judged:

1. Acquired syphilis must be demonstrated in the grandmother and preferably also in the grandfather.
2. Pre-natal as distinguished from acquired syphilis must be demonstrated in the mother of the third-generation case. Acquired syphilis must be excluded in her case and the father must be proved to be healthy.
3. There must be incontrovertible evidence of pre-natal syphilis in the third generation.
4. Manifestations must appear soon after birth in both the second and third generations.

Nabarro (1954), who devoted the greater part of his professional life to the study of congenital syphilis, was firmly convinced that third-generation syphilis did occur and personally observed 42 families with probable syphilis in three generations.

American observers have tended not to regard third-generation syphilis sympathetically, but Beer- man, Wammock, and Magnuson (1942) reported a case in a family group in which they considered that there was sufficient authentic information to permit its classification as a probable case of third-generation syphilis. They also reviewed the case reports published between 1933 and 1941, omitting those reported before 1933, and divided them into more probable and less probable categories, but they could place only seven cases in the first category. Sauer (1951) also reported a case of third-generation syphilis which in his opinion conformed to the Fournier-Finger doctrine as far as it is ever possible to do so, and he urged the continued reporting of cases. In a study of the incidence of neurosyphilis among parents of congenital neurosyphilitic children, Kemp and Poole (1925) were of the opinion that two of the twenty mothers in one of their series showed the stigmata of congenital syphilis and that their children almost certainly represented third-generation syphilis.

More recently, Masterton (1956) has described a case of third-generation syphilis, and this seems to be the last case recorded in Great Britain.

In the same year Szegö (1956) recorded a case and, having reviewed the literature of the subject, commented that up to that time only 68 families conforming to the strict conditions of proof had been described.

The extreme rarity of the condition has prompted me to record the histories of the two following families, which strongly suggest the transmission of syphilis through three generations.

## Case Reports

The clinical data are represented chronologically and not in order of original review. The treponemal immobilization test (TPI) was used throughout the investigation in all living cases wherever relevant. The families have been given fictitious names—Smith and Jones—for purposes of clarity.

### Family Smith (Fig. 1)

**Generation I**

**Maternal Grandmother (28)** (Fig. 1, I, 2)

1922: History of 8 months' swelling of neck glands.

**Clinical Examination.**—Generalized lymphadenopathy, antecubital glands very marked. Gummatous ulcer on left side of neck under lower jaw.

**Blood.**—Wassermann reaction + + .

**Cerebrospinal Fluid.**—No record.

**Treatment.**—She was given neo-arshpenamine and potassium iodide in hospital and after 2·5 g. of the former she developed acute exfoliative dermatitis from which she died 18 days later.
**TWO CASES OF THIRD-GENERATION SYPHILIS**

![Family Tree Diagram](image)

*Fig. 1.—Third-generation syphilis in Family Smith.*

**Obstetric History.**—Two full-term pregnancies. No miscarriages. Her son now aged 6 years, and her daughter 1 year. The blood serology of the children was not apparently investigated at this time in view of the mother's undoubtedly congenital infection.

1955: There was now no perception of light in the left eye. The pupil was widely dilated—she had been applying atropine drops intermittently but not on medical advice. The ocular tension was raised ++.

**Maternal Grandfather** (over 70) (Fig. 1, I, I)

1960: Stated to be alive and in good health and living in Canada where he emigrated after his wife's death.

**Generation II**

**Mother** (35) Mrs. Smith (Fig. 1, II, 5)

August, 1953: Seen at ophthalmic out-patients' department complaining of haziness of vision in the left eye for 6 days. The visual acuity in the left eye was 6/18, and that in the apparently normal right eye was 6/6.

**Blood.**—The Wassermann reaction and Kahn test were both positive ++.

**Treatment.**—Atropine and penicillin eye drops were prescribed.

September, 1953: She was referred to the VD department by the family doctor because of interstitial keratitis and positive blood tests. There was a history of swelling of the right knee joint 2 years previously—somewhat painful at first—less so later on. She admitted that the left knee was also stiff at about the same time.

**Clinical Examination.**—This was negative except for two findings:

1. Mild degree of hydrarthrosis of right knee joint.
2. Moderate amount of sclerosis of left cornea from what appeared to be undoubtedly recent interstitial keratitis.

**Blood.**—The Wassermann reaction and Kahn test were positive ++.

**Cerebrospinal Fluid.**—Not examined.

**Treatment.**—This was started at home with neo-arsphenamine and bismuth, but dermatitis developed after 3·6 g. neo-arsphenamine and 1·6 g. bismuth. Penicillin therapy was substituted but profound anaemia developed; this was a hypoplastic anaemia possibly due to arsenicals or bismuth or both. After several blood transfusions and a radium-induced menopause she recovered and had a further course of penicillin at home.

**Father** (36) Mr. Smith (Fig. 1, II, 6)

1960: There was no history or clinical evidence of present or past syphilitic infection, and he denied any possibility of infection. All blood tests were negative, and it was noted that a previous blood test carried out in 1953 had also been negative.

**Generation III**

**Son** (12) John Smith (Fig. 1, III, 7) (Propositus)

1960: There was a 2 months' history of vague headaches succeeded suddenly by transient loss of consciousness and right hemiplegia affecting particularly the right hand. The following day he complained of severe headache with neck rigidity and photophobia, and was admitted to the neurosurgical unit with left hemiplegia, the hand again being markedly affected. He was confused and strongly resisted attempts at examination.

**Serial Angiograms.**—No intracerebral lesion detected.

**Blood.**—The Wassermann reaction was strongly positive +++++ 1:256.

**Cerebrospinal Fluid.**—Cells 104/c.mm.; Wassermann reaction +++; protein and colloidal gold not estimated.

**Treatment.**—The administration of 500,000 units of crystalline penicillin twice daily for 7 days was followed by remarkable improvement, and after two courses of penicillin to a total of 19·6 mega units, the lumbar puncture was repeated. The cerebrospinal fluid then showed protein 20 mg./100 ml.; cells 8/c.mm.; Wassermann reaction positive; colloidal gold 0011000000.
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Results.—After a further course of penicillin (12 mega units) and two courses of bismuth each of 2 g., the cerebrospinal fluid showed protein 20 mg./100 ml.; cells nil; Wassermann reaction negative; and colloidal gold 0000000.00.

Clinically, apart from a residual extensor plantar response on the left side, there were now no abnormalities. Serological tests showed Wassermann reaction and Price’s precipitation reaction +; Reiter protein complement-fixation test +1:2; treponemal immobilization +. 1963: He remains well and symptom-free, appears to be mentally normal, and is working in a multiple store.

FAMILY JONES (Fig. 2)

GENERATION I

Maternal Grandmother (54) (Fig. 2, I, 2)

1961: Examined in the course of the family follow-up, she was a pale, thin, apathetic woman, complaining of a “bad back for years”.

Central Nervous System.—The pupils were small, approximately equal, but slightly irregular, reacting only slightly to light and contractions not maintained. Both pupils reacted on accommodation. Deep reflexes in the upper limbs were present and equal but were absent on both sides in the lower limbs. Plantar response flexor. Deep pain sensation impaired. Vibration sensation diminished. Romberg’s sign positive.

Cardiovascular System.—No gross abnormalities; x rays of heart and aorta normal.

Spine.—Dorsal scoliosis, concavity to the right. Lumbar kyphosis and scoliosis, concavity to the left. X rays of dorsal spine showed nothing abnormal, but the lumbar spine showed scoliosis of the vertebral bodies of L2, 4, and 5, and almost complete loss of disc space between L1, L2, and L3, and between L4 and L5. There was no evidence of paravertebral swelling. The radiologist described this as a Charcot spine.

Blood.—Wassermann and Price’s precipitation reactions negative; Reiter protein complement-fixation and treponemal immobilization tests positive.

Cerebrospinal Fluid.—Protein 35 mg./100 ml.; cells 2/c.mm.; Wassermann reaction negative; colloidal gold 0000000000.

Obstetric History.—1932 Premature birth—child died after 4 days—cause unknown (Fig. 2, II, 3). 1933 Stillbirth at 8 months’ gestation (Fig. 2, II, 4) 1934 Miscarriage at 6 months’ gestation (Fig. 2, II, 5) 1935 Normal pregnancy and confinement (Fig. 2, II, 6)

Maternal Grandfather (33) (Fig. 2, I, 1)

1939: Stated to have been “queer” for 2 years. Bilateral optic atrophy, trombone tremor of the tongue, diminished pain sensibility, and ataxia. He was certified in March, 1939, and committed to a mental hospital. At that time he was excited, tremulous, drogide, with fluctuating moods, and could not maintain attention.

Blood.—Wassermann reaction and Kahn test positive ++.

Cerebrospinal Fluid.—Protein 125 mg./100 ml.; cells 18/c.mm.; Wassermann reaction ++, colloidal gold 5555553332.

Treatment.—In April, 1939, he had malaria therapy at the mental hospital.

Result.—He died in August, 1939.

GENERATION II

Mother (26), Mrs Jones (Fig. 2, II, 6), only surviving child (Propositus)

1961: Her infancy and childhood were apparently uneventful. She was referred by her family doctor to the VD department because she was found to have strongly positive serum tests in the eighth month of her second pregnancy.

Clinical Examination.—The facies was definitely suggestive of congenital syphilis with wide spacing of the orbits and mild depression of the bridge of the nose with slight flaring of the nostrils. There was a high palatal arch with slight defect in the hard palate admitting the tip of a probe. The patient had artificial teeth but gave without prompting a fair description of Hutchinsonian teeth. She said she had always been self-conscious of her front teeth as a child because they were different from those of other children; she described them as “small and round with jagged edges”.

There was no clinical evidence of involvement of the central nervous or cardiovascular systems, and no abnormality in x rays of the long bones of the limbs, or of the heart and aorta.

Blood.—The Wassermann and Price’s precipitation reactions and the Reiter protein complement-fixation and treponemal immobilization tests were all positive +.

Cerebrospinal Fluid.—Protein 15 mg./100 ml.; cells nil; Wassermann reaction negative, colloidal gold 0000000000.

Treatment.—After three courses of procaine penicillin (PAM) to a total of 42·6 mega units, the serological tests were still positive (Wassermann and Price’s precipitation reactions ++; Reiter protein complement-fixation test +1:16).
TWO CASES OF THIRD-GENERATION SYPHILIS

Father (34) Mr Jones (Fig. 2, II, 7)
1961: There was no history or clinical or serological evidence of acquired syphilis, and he denied any possibility of infection.

Generation III

Son (3), William Jones (Fig. 2, III, 8)
1961: Examined in the course of the family follow-up, he was a bright healthy little boy with no evidence or gross stigmata of congenital syphilis. X-rays of the long bones of the limbs showed no abnormality.

Blood.—The Wassermann and Price’s precipitation reactions and the Reiter protein complement-fixation and treponemal immobilization tests were all positive +.

Cerebrospinal Fluid.—Protein 20 mg./100 ml.; cells nil; Wassermann reaction negative, colloidal gold 000000000.

Son (born 18.8.61), Peter Jones (Fig. 2, III, 9).
Son (born 26.12.62), Douglas Jones (Fig. 2, III, 10).

These were both healthy full-term children, with no clinical evidence of congenital syphilis at birth or subsequently. All serological tests were negative.

Discussion

Congenital syphilis has undergone a profound change in the last thirty years and no longer is it common to see the florid cases of bygone days but rather for congenital syphilis to appear in later years in the form of the late manifestations. It would therefore seem justifiable to modify the Fournier (1891)–Finger (1900) doctrine in the light of present experience of congenital syphilis and in particular the fourth postulate which states that manifestations of congenital syphilis must appear soon after birth in both the second and third generations.

Considering the family histories described, in the first family the maternal grandmother (Fig. 1, I, 2) undoubtedly had syphilis, probably in the benign tertiary stage. There is no evidence as to whether the maternal grandfather (Fig. 1, I, 1) was infected or not. The mother, Mrs Smith (second generation), had evidence of interstitial keratitis in both eyes and positive blood serology. She probably had Clutton’s joints also. The fact that her blood serology was subsequently negative to the standard serological tests, although still positive in the RPCFT and TPI tests, is perhaps unusual but by no means improbable after a lapse of over forty years. The late onset of her symptoms is in keeping with the experience of congenital syphilis nowadays. Laird (1950), discussing the sex and age groups of 45 cases of interstitial keratitis, found that 4 per cent. of female cases did not develop their symptoms until 30–39 years and 6 per cent. did not develop symptoms until 40–49 years. In the third generation case (Fig. 1, III, 7) in this family, the neurological symptoms did not appear till the age of 12 years, the disease having remained latent during the intervening years.

In the second family described, both the maternal grandmother (Fig. 2, I, 2) and grandfather (Fig. 2, I, 1) had neurosyphilis and the maternal grandmother’s obstetric history was very typical. In the mother, Mrs Jones (second generation), the disease had remained inactive throughout and only certain very definite stigmata of congenital syphilis were present. Her persistently positive blood serology in spite of intensive penicillin treatment further substantiated the congenital origin of her disease. Her son William Jones (third generation), although undoubtedly infected, did not show any obvious stigmata or clinical evidence of congenital syphilis, which is in keeping with present-day experience of the disease.

As regards the respective fathers (second generation) of the two probable third-generation cases, the exclusion in them of a syphilitic infection depended on the absence of historical and clinical evidence of infection and the negative blood serology, including negative TPI tests. Sequeira and Wilkinson (1955) have shown that the use of the TPI test appreciably reduces the margin of error in excluding latent syphilis.

The remote possibility of presumably congenitally infected second-generation mothers having been super-infected with the acquired form of the disease has to be considered. Assuming that their respective husbands could with reasonable certainty be cleared of this responsibility, one must assume that super-infection occurred extra-maritally or even by extragenital infection. In the cases under consideration both women denied any possibility of this having occurred and as both seemed entirely reliable witnesses, there seemed no reason to doubt this. Moreover, the comparative youth of one of the second generation mothers would also tend to rule out the possibility of an acquired infection following her congenital infection.

In conclusion, while absolute scientific proof is lacking, the two cases considered do seem to fulfil the Fournier–Finger criteria, allowing for the modification of these criteria in the light of present-day experience of congenital syphilis, and would seem to be probable cases of third-generation syphilis.

Summary

(1) Brief mention is made of some of the published work on third-generation syphilis.

(2) Two family histories in which a syphilitic infection occurred in three generations are described. In both it seemed that the main criteria
of Fournier and Finger were satisfied, allowing for certain modifications of these criteria in the light of present-day experience of congenital syphilis.

(3) The treponemal immobilization test was carried out on all related living members of the families concerned.

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REFERENCES


Deux cas de syphilis à la troisième génération

Résumé

(1) On fait un bref rappel des travaux publiés sur le syphilis à la troisième génération.

(2) L’histoire de deux familles dont trois générations furent atteintes d’une infection syphilitique est rapportée. Dans les deux cas il semble que les principaux critères de Fournier et Finger furent satisfaits, compte tenue de certaines modifications de ces critères dans la lumière de l’expérience actuelle de la syphilis congénitale.

(3) On pratiqua la réaction d’immobilisation du treponème sur tous les membres vivants des familles considérées.
Two Cases of Third-generation Syphilis

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