

Maltese with genetic susceptibility to poliomyelitis: sibs with paralysis at different times

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Abstract

I found the records of 1,072 Maltese cases of poliomyelitis in the islands of Malta from 1909 to 1964. These cases and baptism matched controls were traced to their great grand-parents and all marriages were checked for consanguinity. There were no twins among the polios or controls, but there were 70 pairs of sibs. Of these, 13 pairs suffered poliomyelitis in different epidemics even though the younger sib was born after the elder was paralysed. The 27 pairs of polio sibs were directly related to more than twice as many other polios (through grand-parents and great grand-parents) as the 22 pairs of control sibs. The families of polio sibs contained more consanguineous marriages than either the 21 sibs of which one was a polio and the other a control or the control sibs. The polio sibs provide further evidence of genetic susceptibility to poliomyelitis and possible problems arising from the eradication of the disease.

Keywords

consanguinity, epidemics, genetic susceptibility, Malta, poliomyelitis, sibs

Introduction

In many epidemics of poliomyelitis, researchers have noted a few cases where two sibs have been paralysed, but have ignored the possibility of genetic susceptibility. After 1935 when the 'vaccines' failed, researchers thought that a child with polio excreted more virulent and more virus, thus increasing the risk to the sib. This was not a testable theory. An alternative explanation is that the sibs were genetically susceptible¹⁻² and this is most likely when the sibs were paralysed at different dates and epidemics.

There was an epidemic of poliomyelitis in the Maltese islands in 1918, but no records remain, although the disease was made notifiable. A few cases were reported until the large epidemic of 1942-1943: the last case occurred in 1964. Almost all the cases were in Maltese children under four years, but some were unrecognised at the time and not reported. All adults were immune and babies were protected by maternal antibodies until about six months old. I have found the records of 39 Maltese cases which occurred from 1909 to 1938. Some British children were included in the *Annual Reports*, but others were treated by army doctors and so were unreported.

Method

From 1982 to 1987, with the approval and support of the Chief Government Medical Officer, I examined the notes of the Infectious Diseases Hospital stored in the old Lazarreto on Manoel Island: I found the original notes of 1,072 Maltese cases of poliomyelitis from 1909 to 1964. I looked at, and noted only the information of name and date of birth of the child. The records have since been trashed by unknown intruders. I also checked the names against the original physiotherapy notes at St. Lukes Hospital as well as some notes of cases prior to 1926 when seen for orthopaedic care. With the approval and support of the Public Registrar (a lawyer), the Archbishop of Malta, the Bishop of Gozo and the kappillans (parish priests), I traced their parents, grand-parents and great grand-parents, together with baptism matched controls, from the public parish birth and marriage records, as well as the Public Registry where necessary. Polios and controls were allotted to the parishes of their great grand-parents. I have traced more

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than 4,500 births and 16,000 marriages. The Vatican dispensations for consanguinities of marriages were noted. Details of cases or controls were entered on cards and all names were entered alphabetically for each parish or village and these were also amalgamated as far as possible.

This is the first study to find all the cases of poliomyelitis in a large population over many years, rather than unconnected studies of individual epidemics or individuals.

Results

After the polio epidemic of about 430 Maltese cases in 1942-1943 in Malta and Gozo, Professor Seddon of Oxford University was flown to the island and examined all the cases. He noted six pairs of sibs with paralysis³ to which I have added three more pairs in which the paralysis of the younger sib was only recognised later (my records). I have found a further 18 pairs of polio sibs: among four pairs, both were paralysed at the same time, but 14 pairs were affected in different epidemics. In 13 cases the younger was born after the elder was paralysed and in one village the elder was not infected in the 1942 epidemic, but was paralysed later. The younger sibs were born from five months to 11 years after the older was paralysed. In one case, the family had moved house before the younger sib was born 11 yr after the elder was paralysed (Table 1)

Table 1: Pairs of sibs with polio who were paralysed at different times in Malta and Gozo

| | Related to | Consanguinity |
|--|--|-----------------------------------|
| Case 862 was born years after the elder sib, 415 was paralysed | via paternal ggp to 889, ggp to 424 and via g-ggp to 5 other polios | via maternal |
| Case 875 was born years after the elder sib 700 was paralysed | via ggp to 918, 1034, 1063 | parents II + III, paternal gp IV |
| Case 610 was born more than 1 yr after the elder sib 244 was paralysed | via paternal ggp to 243 | maternal gp IV |
| Case 1024 was born years after elder sib 297 was paralysed | father related to 3 polios in Mellieha | |
| Case 650 was born years after the elder sib 250 was paralysed | | parents III |
| Case 696 was born years after the elder sib 143 was paralysed | | [mother from Europe] |
| Case 6 was born years after the elder sib 5 was paralysed | | [family had moved to a new house] |
| Case 1100 was born years after the elder sib 1100B was paralysed | | maternal gp II |
| Case 809 was born years after the elder sib 179 was paralysed | via mother's nephew to 157, and mother's niece to daughter 767 | paternal gp II |
| Case 669 was born after the elder sib 382 was paralysed | via paternal gp to 736 and ggp to 149, via maternal ggp to 788 | |
| Case 803 was born years after the elder sib 357 was paralysed | via maternal gp to 910, and ggp to 175 and via paternal gp to 12 and 111 | |
| Case 880 who was born in 1929 was paralysed at 22 yr, 8 yr after a younger sib 144 was paralysed | via maternal ggp to 630, via mother's niece to 701 | maternal gp IV |
| Case 683 was born after the elder sib 346 was paralysed | | |
| Case 745 was born after the elder sib 699 was paralysed | | |

gp: grand-parent ggp: great grand-parent

The 27 pairs of polio cases were related through grand-parents and great grand-parents to another 33 polios, more than twice as many as those related to the 22 pairs of control sibs (Table 2). The families of polio sibs contained more consanguineous marriages of parents and grand-parents than either the 21 pairs with a polio and a control or the 22 control pairs (Table 3). With the small numbers involved, these differences might be due to chance (Fisher's Test) although all point to a difference. In the 21 pairs of sibs with polio and control children, the control might be genetically a 'polio' who did not develop paralysis either because the poliovirus was less virulent than in other epidemics or because the child was not yet sufficiently primed.⁴

Table 2: Pairs of sibs in Malta and Gozo

| | Nos. | Connected to | | | | Consanguinities | |
|-------------------------|------|--------------|--------|----------|------|-----------------|---------------|
| | | others | polios | controls | none | parents | grand-parents |
| Both sibs polios | 27 | 16 | 33 | 15 | 11 | 4 | 7 |
| one polio + one control | 21 | 10 | 8 | 6 | 11 | 1 | 5 |
| both controls | 22 | 12 | 16 | 14 | 10 | - | 3 |

Table 3: Histories of consanguinity among pairs of sibs in Malta and Gozo

| | Nos. | Consanguinities | | | | | | | |
|-------------------------|------|-----------------|-----|----|--------|---------------|--------|----|--|
| | | parents | | | | grand-parents | | | |
| | | II | III | II | II/III | III | III/IV | IV | |
| Both sibs polios | 27 | 2 | 2 | 3 | | | 1 | 3 | |
| one polio + one control | 21 | | 1 | | 1 | 2 | | 2 | |
| both controls | 22 | | | | | 2 | 1 | | |

Of the nine pairs of sibs who were paralysed in the 1942-1943 epidemic, four pairs were from Malta, but five pairs occurred on the small sister island of Gozo: #465 and #467, #180 and #493, #158 and #159 with #207 and #564, and #468 and #469 in Victoria. Gozo had a population one tenth that of Malta.

In one small isolated village there were eight cases of polio and another case where the mother came from a different village (Wyatt, in preparation). In this village there were two pairs of sibs with paralysis at different times. On the island of Malta, there were 956 polio cases of which 54% were related as sibs and first and second cousins (Wyatt, in preparation). On the smaller island of Gozo, which had a greater proportion of consanguineous marriages than Malta (paper submitted), of the 116 cases, 67% were related as sibs and first and second cousins.¹⁰

Discussion

In his Report of the 1942 Malta epidemic Seddon commented: '...result of exposure to small doses of virus sufficient to confer immunity without producing more than an occasional case of definite paralysis. But many children under 5 and some under 10, had failed, either through lack of exposure or because of some intrinsic defect, to become immunised'.³ There was no explanation of what an 'intrinsic defect' could be or how this minimal exposure over the previous twenty years had suddenly changed, but only for the young children. That the Maltese cases were only small children shows that over the years almost everyone in the islands had been infected by successive waves of virus: there were, however, 58 cases among the adult British servicemen³. In later epidemics, all save one of the Maltese cases had been among the thousands of children born since the previous one.

There were no entries for sibs in the extensive 93 page subject index of the bibliography of poliomyelitis⁵, nor in Paul's wonderful history of polio.⁶ In his chapter on Aycock, Paul did not mention Aycock's fascination with a genetic background to polio or his many papers with examples of families with multiple cases. In discussing this chapter with Paul, I asked why he had omitted the papers on genetic susceptibility. Paul had no memory of them, but later wrote to me that he had found his letter to the Rockefeller Foundation in which, as a referee, he had advised against a grant to Aycock to study genetic susceptibility. Paul would have considered the search for a vaccine to be the priority. Wickman gave many examples of sibs who had suffered attacks in epidemics, but did not distinguish between those with permanent paralysis and those who recovered ie, non-paralytic.⁷ Other papers of genetic susceptibility to polio are discussed in ref. 4.

Burnet in a lecture in America said that 'there is good reason to believe that paralytic polio and overt tuberculosis depend more on the presence of individual genetic susceptibility to an initial infection than to the virulence or dose of the infecting strain'.⁸ No references were given in this paper, but the only source of this belief is likely to be mine in *Medical Hypotheses* where Burnet was prominently displayed as one of the five Advisory Board.^{4,9}

Conclusion

Although genetic susceptibility has been ignored for 100 years and WHO says that only 1 in 200 is paralysed, one in 50 was paralysed in dozens of epidemics.⁹ In 1948 a virgin soil epidemic affected two out of 53 Inuit children and 26 % of the adults: Sabin interpreted this to be 'an isolated highly inbred population of special genetic susceptibility', but failed to recognise that the Hardy-Weinberg ratio was

2% p^+p^+ 24 % p^+p^- and 74% p^-p^- [see ref. 4]. How could genetic susceptibility be confined only to an Inuit group? How can strains of different virulence only cause paralysis to the same proportion of cases (up to 2 % in very young children and up to 24% among adolescents and adults) unless there is an underlying genetic susceptibility? In epidemics due to importation of poliovirus from Egypt by eg British servicemen in 1942 and Maltese soldiers and dockyard workers in 1945 and 1947, when everyone was infected, the same families suffered children with paralysis. My study shows that many cases of genetic susceptibility occurred in the large population of more than 300,000 Maltese.¹⁰

Genetic susceptibility for poliomyelitis in populations has been ignored.¹¹ but familial cases and pairs of sibs with polio, provide ample evidence for it and the need for realistic planning for the post-eradication age. When ten years elapse without a case of poliomyelitis, immunisation will cease. After that time, two per cent of children will then be at risk without immunity should a virus reappear. But ten years later, there will be cohorts of young people of whom up to 24 % will be at risk of paralysis. When polio cases no longer occur and immunisation ceases, there will still be a danger that a polio or polio-like virus may emerge. Polio or similar viruses may escape from unsuspected sources in laboratories, may be deliberately manufactured, may mutate from other enteroviruses or may have lain dormant in the environment. Plans must be made for the possibility that many with genetic susceptibility and no immunity might be infected. It will be prudent to have stocks of vaccine available for an emergency, but the knowledge that so many people might be susceptible to paralysis demands that far larger stocks of vaccine than presently envisaged may be required.

I have arranged that all the notes, cards, printouts etc will be deposited with the Melitensis Collection of the University of Malta where they will be available to those with permission from the Medical Ethics Committee. I am grateful to the Royal Society for a travel grant in 1985 and to all those kappillans and doctors who helped me.

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