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# Heredity and Infectious Diseases: A Twin Study

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**Abstract**. A concordance study of 6 infectious diseases of childhood has been carried out in a sample of 656 twin pairs classified by sex and zygosity. A new approach is proposed to estimate the respective influence of heredity and of common environment. The estimates thus obtained range from 86% hereditary component in the case of measles to 100% environmental component in the case of scarlet fever.

**Key words**: Measles, Mumps, Chickenpox, German measles, Scarlet fever, Whooping cough

Interest in the role of genetic factors in infectious diseases persists over the years as shown, for istance, by a recent [2] case report and survey of the literature on the subject of endouterine cytomegalic viral infection in twins, amounting to a total of three known cases: one concordant MZ and two variously discordant DZ pairs.

The influence of genetic factors in infectious diseases has interested us for a long time and in the following we shall report on the results of a questionnaire study we have recently conducted.

Table 1 shows the size of our sample by sex and zygosity. A total of 656 pairs (71 of which of unknown zygosity) have so far filled out our questionnaire, submitted to about 1000 pairs of twins aged 18 to 25 from our file at the Mendel Institute. The questionnaire referred to the following infectious diseases: measles, mumps, chickenpox, German measles, scarlet fever, and whooping cough (Table 2).

The Figure summarizes graphically the proportions of concordant pairs (both affected), discordant pairs (affected vs healthy), and nonaffected pairs (both healthy) that we found, for each individual disease, in the two zygosity groups, MZ and DZ, and in Random Pairs (RP). The latter were derived as follows: for each pair, the identification,

Table 1 - The Sample

| Sex | MZ | DZ | UZ | Total |
|---|---|---|---|---|
| MM | 85 | 108 | 26 | 219 |
| MF | | 154 | | 154 |
| FF | 114 | 124 | 45 | 283 |
| Total | 119 | 386 | 71 | 656 |

Table 2 - Presence (P) and Absence (A) of Infectious Diseases in Twin Pairs According to Zygosity

| | MZ | DZ | UZ | Total | | MZ | DZ | UZ | Total |
|---|---|---|---|---|---|---|---|---|---|
| **Measles** | | | | | **Mumps** | | | | |
| P × P | 78 | 160 | 31 | 269 | P × P | 40 | 96 | 16 | 152 |
| P × A | 17 | 42 | 11 | 70 | P × A | 15 | 19 | 2 | 36 |
| A × P | 15 | 37 | 6 | 58 | A × P | 15 | 42 | 12 | 69 |
| A × A | 89 | 147 | 23 | 259 | A × A | 129 | 229 | 41 | 399 |
| Total | 199 | 386 | 71 | 656 | Total | 199 | 386 | 71 | 656 |
| **Chickenpox** | | | | | **German Measles** | | | | |
| P × P | 50 | 116 | 16 | 182 | P × P | 20 | 29 | 4 | 53 |
| P × A | 6 | 34 | 9 | 49 | P × A | 7 | 24 | 3 | 34 |
| A × P | 14 | 26 | 6 | 46 | A × P | 1 | 21 | 5 | 27 |
| A × A | 129 | 210 | 40 | 379 | A × A | 171 | 312 | 59 | 542 |
| Total | 199 | 386 | 71 | 656 | Total | 199 | 386 | 71 | 656 |
| **Scarlet Fever** | | | | | **Whooping Cough** | | | | |
| P × P | 5 | 6 | 2 | 13 | P × P | 52 | 80 | 11 | 143 |
| P × A | 8 | 14 | 3 | 25 | P × A | 12 | 9 | 3 | 24 |
| A × P | 4 | 8 | 1 | 13 | A × P | 11 | 20 | 2 | 33 |
| A × A | 182 | 358 | 65 | 605 | A × A | 124 | 277 | 55 | 456 |
| Total | 199 | 386 | 71 | 656 | Total | 199 | 386 | 71 | 656 |

Twin 1 and Twin 2, was assigned at random. The individual frequencies of each of the six diseases were then calculated for all of the Twins 1 and all of the Twins 2, and the average frequency was used to derive expected distributions of concordance and discordance on the hypothesis of independence, ie, in Random Pairs (RP).

We assumed that discordance values would be lower in DZ than in Random Pairs on account of similar environment and similar genotype in the former, and lower in MZ than in DZ pairs as a result of the identical genotypes of the former. On these assumptions, we developed a method, outlined in Table 3, to estimate heritability (H) as well as the effect of the shared environment (Es). When applied to the discordance frequencies obtained in our sample, this method leads to the estimates of Es (shared environment) and H (heritability) that are shown in Table 4.

**Table 3 -** Method for the Estimate of Shared Environment Effect ($E_S$) and of Heritability (H) from Discordance Frequencies

$$\left\{ RP \neq - DZ \neq \right\} = f(E_S) + f(1/2 \, H)$$

$$\left\{ DZ \neq - MZ \neq \right\} = f(1/2 \, H)$$

$$\left\{ (RP \neq - DZ \neq) + (DZ \neq - MZ \neq) \right\} = f(E_S) + f(H)$$

$$\left\{ (RP \neq - DZ \neq) - (DZ \neq - MZ \neq) \right\} = E_S$$

$$\left\{ 2(DZ \neq - MZ \neq) \right\} = H$$

$\neq$ Discordant pairs          RP = Random pairs

**Table 4 -** Estimates of Shared Environment Effect ($E_S$) and of Heritability (H)

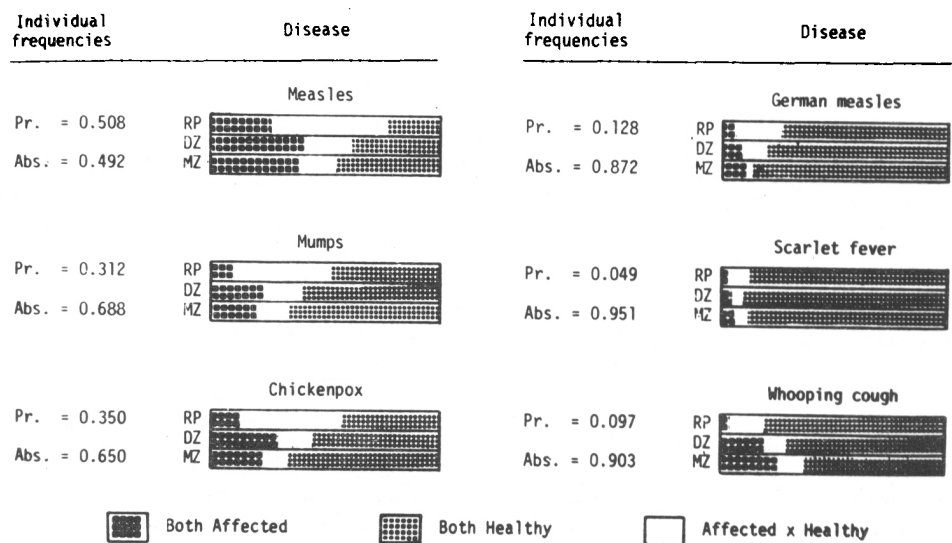| Disease | Discordance frequencies | | | Estimate (%) | |
|---|---|---|---|---|---|
| | RP | DZ | MZ | $E_S$ | H |
| Measles | 0.500 | 0.205 | 0.161 | 74.56 | 25.44 |
| Mumps | 0.429 | 0.158 | 0.151 | 94.96 | 5.04 |
| Chickenpox | 0.455 | 0.155 | 0.100 | 69.08 | 30.92 |
| German measles | 0.223 | 0.119 | 0.040 | 13.66 | 86.34 |
| Scarlet fever | 0.093 | 0.060 | 0.060 | 100.00 | 0.00 |
| Whooping cough | 0.169 | 0.075 | 0.115 | ? | ? |



**Figure -** Concordance and discordance in MZ and DZ pairs vs. random pairs (RP).

Although caution is obviously needed, taken at face value these results point to a role of a genetic factor that appears to be highest in the case of German measles, still relevant in the case of chickenpox and measles, and pratically nil for the other infectious diseases considered.

That genetic factors do play a role in infectious diseases should not be surprising when one considers, for instance, that DZ twin fetuses, although clearly exposed to identical endouterine conditions, may be discordant for a cytomegalic viral infection, as observed by Morton et al [2] and referred to at the beginning of this paper. If individual genetic difference and fetal autonomy can differentiate the twins' response to the same infectious agent under identical endouterine conditions, then it is likely that the role of genetic factors in postnatal infectious diseases can even be greater.

## REFERENCES

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