

February 21, 1957

Professor P. B. Medawar, F.R.S.
University College, London
London, England

Dear Professor Medawar:

I thought the enclosed manuscript might perhaps interest you.

I am looking forward to seeing you at the New York meeting.

Sincerely,

Leo Szilard

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Encl.

UNIVERSITY COLLEGE LONDON

DEPARTMENT OF ZOOLOGY

Telephone : EUSton 7050

Professor P. B. Medawar

GOWER STREET WCI

29 Sept 1959

Dr Leo Szilard,
c/o Dr R.B.Livingstone,
National Institutes of Health,
Bethesda 14, Md.,
U.S.A.

Dear Szilard,

It was great fun seeing you again last night, and I'm so glad you were able to come. The two men you met, in case you haven't a note of their names, were David Newth (embryology) and John Maynard Smith (genetics) — both lively members of this department.

I have written to Professor Peter Krohn (Anatomy Department, Medical School, University of Birmingham, Birmingham 15) asking him to send you a copy of his paper on the experimental analysis of ageing.

Sex ratio. In England and Wales in 1956 the following children were born to mothers of the following ages:-

	boys	girls	ratio
under 20	19647	18291	107.4
20-24	105121	98772	106.4
25-29	114402	108318	105.6
30-34	73320	69656	105.3
35-39	36335	34663	104.8
40-44	10373	10113	102.6
45-49	678	634	106.9
all ages	359881	340454	105.7

105.7
1.8
1.5
23
H

Before taking these data at their face value there are various standard catches to bear in mind, e.g. (a) some 25% of women under 20 are pregnant at marriage and marry partly for that reason, so they may represent an atypically fertile group; (b) the age-groupings are heterogeneous with respect to social class or occupation and may thus be genetically non-random: generally speaking "lower class" women marry younger.

However, the trend of the figures is too bold to make one discount their significance on these grounds.

The most recent analyses I know are:-

- J.LEJEUNE & R.TURPIN C.R.Acad.Sci., Paris, 244: 1833.
E.NOVITSKY & L.SANDLER Amer.J.Human Genetics 21: 123, 1956.
E.NOVITSKY & A.W.KIMBALL Ibid. vol 10, 1958.

The general impression seems to be that paternal age is the main determining factor but that maternal birth order (not age) is also probably relevant.

Incidentally, in view of what you were saying last night, it's very relevant that the human Y-chromosome seems to be relatively much more important than the Drosophila Y-chromosome. Thus an XO human being is not a normal male: the external genitalia are feminine but grossly underdeveloped (Turner's syndrome, gonadal aplasia); and an XXO human being is not a normal male, but has small and almost aspermic testes. There's a summary of these facts, with references, in J.A.Fraser Roberts' Introduction to Medical Genetics, 2nd ed., 1959, pp.252-3 (London, Oxford U.P.).

In general, there is an almost inexhaustible goldmine of information in human actuarial and fertility statistics (particularly in this country and Sweden).

I hope it won't be too long before we meet and chat again.

Yours ever,

Peter Medawar.

5% in 24 years

2 bits

9%



November 11, 1959.

Professor Peter Medawar
Department of Zoology
University College London
Gower Street
London W.C. 1.

Dear Medawar:

Please excuse my delay in thanking you for your very kind letter of September 29th. I got snowed under upon my return to America and I am working against a deadline trying to finish two papers prior to submitting to some surgery, which might put me out of circulation for a few weeks. I shall take the liberty of sending you preprints of these papers as soon as I manage to get them into a shape at which preprints can be made.

The data which you sent me in your letter are quite similar to the data which I had in my files, taken from U.S. vital statistics, but so far all these data are based on rather small numbers, far too small for comfort. In view of the small samples on which the data in your letter are based, it is rather surprising that the ratio of boys and girls falls as smoothly with the mothers' age as it does. Having made this reservation I may now say the following:

According to my theory of aging we should expect an average of one hit per haploid set of chromosomes of the somatic cells, in a period of 12 years. The length of the Y chromosomes amounts to 2 % of the total length of the haploid set of the autosomes (and on this basis we may perhaps assume that an average of 2 % of the Y chromosomes of the spermatogonia suffer an aging hit in a 12 year period. On this basis we are then led to conclude that the ratio, at birth, of boys and girls should decrease by 2 %, for a 12 years increase in the age of the father.

This conclusion is based on the following notions: If the X chromosomes in a spermatogonium suffers an aging hit, the cell is eliminated. If the Y chromosomes in a spermatogonium suffers an aging hit, the cell remains fully functional and will give rise to spermatozoa, but only to spermatozoa which contain an X chromosome.

On the basis of the above reasoning we should expect ~~for~~
~~a 24 year period~~ a 4 % decrease in the ratio, at birth, of boys
and girls, for a 24 years increase in the age of the father.

The data contained in your letter give for this ratio
107.4 for mothers under 20, and 102.6 for mothers between 40 and
44 years of age. In view of the small samples involved I should
not have expected such a close fit of the experimental and
theoretical values.

If you should happen to come across data which are based
on larger samples, I should greatly appreciate your dropping me
a line. I am playing with the idea of sending a note to Nature
on this subject when I get around to do so. Do you think that I
should?

With kindest regards,

Sincerely,



Leo Szilard

UNIVERSITY COLLEGE LONDON

DEPARTMENT OF ZOOLOGY

Telephone : EUSton 7050
Professor P. B. Medawar

GOWER STREET WCI
16th November 1959.

Dr. Leo Szilard,
The Enrico Fermi Institute for Nuclear Studies,
The University of Chicago,
Chicago, 37,
Illinois,
U.S.A.

Dear Szilard,

Very many thanks for your letter. Your interpretation of the drop in the sex ratio makes excellent sense to me, and I think it would be very much to the point if you were to write a letter to Nature.

The catch about getting samples of adequate size is that, in most countries, odd though it may seem, the age of women at the birth of their children is not recorded. I don't know what the situation is in America, but here we only started it in 1938. I could certainly let you have the annual data for the past 10 years for pooling — though your Department of Social Studies or History is bound to have the relevant documents — viz. Part 2 (Tables, Civil) of "The Registrar-General's Statistical Review of England and Wales", which is issued annually.

There are the usual statistical catches about taking these data at their face value — one of them being that the women over 40 who are still having children are quite likely to be an unrandomly fertile sample of the general population.

I don't like hearing about this operation of yours, but wish you all good luck with it — I hope it is only a minor matter.

All good wishes,

Yours ever,

Peter Medawar

P.S. Some time you must tell me how large a sample you would like — there are usually less than $\frac{3}{4}$ million births annually in this country, so I don't think you are ever going to get very large numbers for the over-40's.