VITAMIN E AND HABITUAL ABORTION

BY

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Claims for the successful use of wheat-germ, wheat-germ oil, and concentrates prepared from wheat-germ oil have been criticized because of the absence of adequate controls. Thus in 1937 it was legitimate to write: "It is necessary to refer . . . to a general difficulty in assessing the results of treating habitual abortion with vitamin E preparations. There do not appear to be available any statistics showing the number of full-term births that would be expected in a group of, say, 100 untreated women who had had two or more successive miscarriages" (Bacharach, 1937). I went on to mention the figure of 75 per cent. of live births reported in most groups of habitual abortants who had undergone vitamin E therapy and to express the view that the available facts were "suggestive that vitamin E has specific uses in cases of this kind."

Malpas's Investigation

Two years later Vogt-Möller (1939), though himself convinced of the value of vitamin E in treating this condition, wrote: "There does not appear to be any information regarding the number of full-term births that might be expected in a group of untreated women with a past history of two or more successive 'spontaneous' miscarriages." At this time Vogt-Möller could obviously not have been aware of an interesting paper by Malpas (1938), who applied statistical methods to the problem in question. He had found 18 per cent. of abortions in 2,000 fraternities examined—a figure very close to those of Whitehouse (17.6 per cent.) and Mall (20 per cent.), both quoted in his paper. In a study of 115 abortion and stillbirth sequences he found that eighty-four had had three or more consecutive failures, and further analysis led him to the conclusion that the chances of full-term pregnancies in untreated cases could be fairly accurately expressed as follows:

After two successive abortions	62 per cent.
" three " " " " " "	27 " "
" four " " " " " "	6 " "

Malpas then went on to compare these expected rates with the results reported by Watson and Tew (1936): there were 30 per cent. of failures among seventeen treated cases that had had two or more successive abortions. Malpas doubts whether this departs significantly from the figure shown by the table of expectations, and concludes: "It would appear that while the experimental evidence for the role of vitamin E in the maintenance of pregnancy is impressive, the clinical results are far from convincing."

Analysis of Published Figures

Following the appearance of Malpas's paper opportunity has been taken to re-examine not only the results given by Watson and Tew (1935), who have published a slightly longer list than that quoted by Malpas, but also the series of cases reported by Vogt-Möller (1931, 1933, 1936). In making this comparison, however, it was necessary to consider critically Malpas's analysis as well as the case records published by the Danish and the Canadian authors. All cases have been eliminated in which any full-term infants had been born, because it seems that Malpas's figures are strictly applicable only to consecutive unsuccessful pregnancies. Also a slight adjust-

ment has been made in Malpas's expectancy figures. The one woman in a hundred who always aborts is outside the chance scheme, and allowance must be made for this in calculating the expectation. This has been done in the sixth column of the table. There is also internal evidence in his paper for the belief that this figure of 1 per cent. is too low; if it is, then the expectancy rates would have lower values than those given in column 3, Table I, of his paper. This lowering would tell in favour of therapy when comparison is made between treated and untreated cases; any test of the effect of therapy is therefore made more stringent by accepting his figure of 1 per cent., which has been done in tabulating the comparisons in the accompanying table.

Further, in Malpas's original tables the figures of 62 per cent., 27 per cent., and 6 per cent. refer to women who have aborted in the first two, the first three, and the first four pregnancies respectively; in the table the corresponding figures for treated cases are for women who have had two or more, three or more, and four or more abortions. The comparison is therefore obviously weighted in favour of the untreated cases.

Treatment of Habitual Abortion with Vitamin E

No. of Previous Abortions	Vogt-Möller		Watson and Tew	Total per cent. (Weighted)	Expectation Rate	Chances
	Series I	Series II				
4 or more	6/6 (100%)	21/29 (72%)	6/7 (86%)	79% (33/42)	6.5%	About 1 in 10 ⁶
3 " "	8/9 (89%)	30/43 (70%)	10/14 (71%)	73% (48/66)	27.6%	About 1 in 10 ⁴
2 " "	9/11 (92%)	38/52 (73%)	22/29 (76%)	75% (69/92)	61.7%	About 1 in 200

Columns 2, 3, 4, and 5.—The figures in parentheses indicate the percentage of cases; the left-hand figures the number going to term, the right-hand figures the number treated.

Column 6.—These are Malpas's figures adjusted in the manner described.

Column 7.—These are the probabilities that, owing to chance alone, the percentage of full-term births recorded would differ from the expectancy rates by as much as, or more than, the actual differences found.

There seems, from this analysis, to be little doubt that sources of vitamin E had a direct effect in making possible full-term births among women who had had two or more consecutive abortions or miscarriages.

Species Requirements of Vitamin E

For mice and rats the vitamin is essential to normal reproduction. In its absence certain species—rat, guinea-pig, rabbit, and dog—have been shown to develop a characteristic muscular dystrophy. Its successful use in the veterinary treatment of cows and sows has been claimed, particularly by Vogt-Möller. There seems little doubt that it is needed for normal production and hatchability of hen's eggs. Certain American workers (Thomas *et al.*, 1938) claim, however, that its absence does not prevent normal pregnancy in the goat, the sheep, and the rabbit.

There can therefore be no conclusion on general grounds as to its indispensability to the human species, but it is suggested that the analysis given in this paper affords at least presumptive evidence that it is needed for normal pregnancy in women.

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