

Mongolism, Delayed Fertilization and Human Sexual Behaviour

GERMAN¹ has put forward an interesting hypothesis to account for the increased incidence of mongolism among the offspring of mothers more than 35 yr old. He maintained that the frequency of coitus decreases with age², and so therefore does the proportion of time during which fresh spermatozoa are present in the uterine tube. Thus oocytes, which in younger women might be fertilized immediately after release into the uterine tube, may in older women be fertilized only after several hours. During that time deterioration of the oocyte may occur, one possible effect being the production of a mongol child. It is worthwhile examining this hypothesis more closely using rough estimates of the length of life of the oocyte and of the sperm (given as 24 h and 48 h, respectively, by German).

Taking the simplest possible model, in which the frequency of coitus declines with the age of the woman, but is constant for all women of a specific age: according to German's hypothesis there will be no difference in the incidence of mongolism among the offspring of women for whom the interval between successive coiti is less than the life of the sperm (48 h), because there will always be sperm available. Nor will there be any difference in the incidence of mongolism among couples for whom the interval is greater than the life of the sperm plus the life of the oocyte (72 h). Any prolongation of the interval between coiti will merely add to the length of time when neither sperm nor oocyte is present in the uterine tube. Thus the incidence of mongolism will, on this simple model, change only between maternal ages corresponding to the intervals of 48 h and 72 h.

These intervals correspond to frequencies of coitus of 3.5/week and 2.33/week. Kinsey *et al.*² quote mean rates of 3.7/week for the age group 16-20 yr, and 2.3/week for the age group 31-35 yr, so the incidence of mongolism should change only up to the maternal age of 35 yr. Using the median rates quoted by German would give a corresponding upper limit of about 30 yr.

Admittedly the model is artificial. The assumption most likely to be seriously in error is that the deterioration of the oocyte will be spread over the whole of the 24 h life span. One would expect natural selection to favour a situation in which deterioration and death took place rapidly, that is, at the end of the 24 h period. If this is so, then the hypothesis becomes even less tenable.

If we suppose that deterioration of the oocyte takes place during the last x h, then the change in incidence will take place between the ages corresponding to intervals between coitus of $(72-x)$ h and 72 h. Thus if x were 7.4 the change should occur, on the basis of the figures of Kinsey *et al.*², between the ages of 26 and 35 yr. The smaller the value of x , the smaller the age range over which the change in incidence will occur.

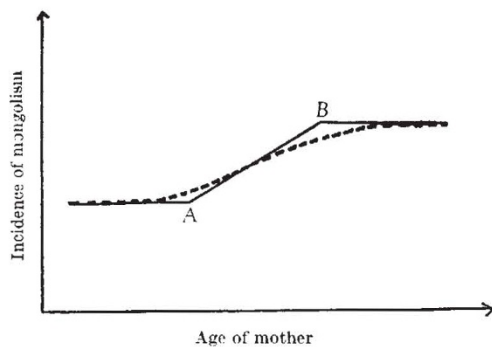


Fig. 1. The shape of the segment AB is determined by the way in which the oocyte deteriorates, and the manner of decline of coital frequency with the woman's age. For convenience a straight line is shown. —, a ; ---, b .

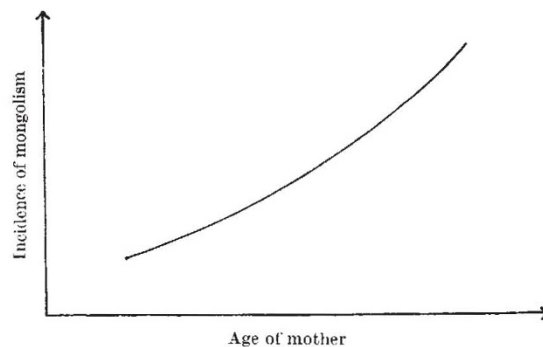


Fig. 2.

In practice one should take into account both the variability between couples, and that within couples. Kinsey *et al.*² report the latter to be small, while the former may be appreciable. This will have the effect of extending the age range in which the change occurs. The greater the variability the greater the spread, and the effect will be to convert an incidence curve such as Fig. 1a (representing the simpler model here) to one such as Fig. 1b.

These diagrams do not agree well with known rates of incidence of mongolism for various ages. Incidence figures quoted by Roberts³ are 1 in 2,000-2,500 for mothers under 30 yr old, 1 in 1,200 for 30-34 yr, 1 in 300 for 35-39 yr with a progressively steeper rise after that (as in Fig. 2).

This discrepancy seems to suggest that additional factors are at work, which have as a whole a greater influence on the incidence of mongolism with age than that hypothesized by German. A longer period of degeneration of the oocyte among older women, or a shortening of the life of the spermatozoa from their partner, are possible explanations.

Although these models are, at best, crude approximations, they seem to indicate that the hypothesis is not sufficient to explain the change in incidence of mongolism with maternal age.

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¹ German, J., *Nature*, **217**, 516 (1968).

² Kinsey, A. C., Pomeroy, W. B., Martin, C. E., and Gebhard, P. H., *Sexual Behaviour in the Human Female*, 348, Table 93 (W. B. Saunders and Co., London, 1953).

³ Roberts, J. A. F., *An Introduction to Medical Genetics*, 170 (Oxford University Press, 1963).

Exercise Proteinuria and Proteinuria induced by Kallikrein

EXERCISE proteinuria was first reported¹ in 1878, and since then increased excretion of protein in the urine during and after exercise has been extensively studied. The physiological mechanisms involved, however, remain unknown. We have found that not only did the activity of kallikrein in urine increase after exercise, but that intravenous administration of urinary kallikrein could induce experimental transient proteinuria in rabbits². It therefore seemed to be relevant to the causes of exercise proteinuria to examine the mechanisms of proteinuria induced by urinary kallikrein.

To examine the effect of heavy muscular exercise on kallikrein activity and the excretion of protein into the urine, we took urine samples from five healthy subjects at rest, just about to run, while running and 30 min after running. Urinary kallikrein was prepared as follows. Human urine taken before and after exercise was mixed with four volumes of cooled ethanol and centrifuged at 1,000g for 10 min after standing for 1 day in the