LETTERS TO THE EDITORS

The Editors do not hold themselves responsible for opinions expressed by their correspondents. No notice is taken of anonymous communications.

Sensitivity of Immature Mouse Sperm to the Mutagenic Effects of X-Rays

DR. A. J. BATEMAN'S careful analysis of X-ray-induced dominant lethality in the mouse[1] has yielded a sequence of mutation frequencies in successive matings which is strikingly similar to that of *Drosophila*, as established by me[2] and Khishin[3] for recessive lethals. In the mouse, as in *Drosophila*, successive matings of irradiated males result in an initial drop in frequency of mutation, followed by a pronounced peak, which in turn is followed by a decline to about the initial value and finally to a very much lower level. The initial drop, which in *Drosophila* takes place between the first and the second day, has been variously interpreted as due to a difference of sensitivity between fully mature and nearly mature spermatozoa[4,5] or as recovery from genetical X-ray damage during the first 24 hr. after irradiation[6,7]. Both interpretations are possible for the parallel drop in the mouse which, according to a personal communication by Dr. Bateman, is entirely due to an excess of dominant lethals on the first day.

A further analysis of the sensitivity pattern of the testis has been possible in *Drosophila*, where induced crossing-over and the formation of bunches of identical cross-overs can be used as markers for the treated stages[2] and where, moreover, irradiation of larvæ and pupæ allows a cytological check on the stage treated[3]. It has been inferred that maximal sensitivity occurs late in spermiogenesis, when spermatids become transformed into spermatozoa, that meiotic stages and young spermatids are about as sensitive as mature sperm, and spermatogonia much less so.

A similar analysis is not possible in the mouse, where crossing-over in the male occurs even without irradiation. One may, however, draw some conclusions on the stage treated from the time after irradiation at which aspermy or oligospermy occurs. A number of workers, most recently Oakberg[8], have shown that type *B* spermatogonia are by far the most easily destroyed stage, and that meiotic cells are much more resistant. With the low X-ray dose used by Dr. Bateman, spermatocytes are probably not killed—although their development may be somewhat delayed—and the oligospermic matings during the sixth and seventh week almost certainly represent irradiated late spermatogonia. The few dominant lethals which occurred during these weeks may have been due to admixture of spermatozoa treated during meiosis; there is also no reason for assuming that every dominant lethal which occurred in a spermatogonium must be eliminated in meiosis. On this interpretation, meiotic and early post-meiotic stages, sampled in weeks 4 and 5, are about as sensitive to the mutagenic effects of X-rays as mature spermatozoa, and the peak of mutation-frequency occurs at a late stage in spermiogenesis, as it does in *Drosophila*. At higher doses also spermatocytes are killed, and this—not killing of the very resistant spermatids[8]—explains why males given 500 r. became sterile already in the fourth week.

Dr. Bateman's interpretation of his findings is different. In his opinion, the sensitivity pattern to the mutagenic action of X-rays differs fundamentally between the mouse and *Drosophila*. There are two reasons for his belief. One is the assumption that in the mouse, as in *Drosophila*[2,9], spermatocytes are very easily destroyed by radiation: this results in an interpretation of the dominant lethal curve of the mouse which, in my opinion, is incorrect. The second is the assumption that in *Drosophila* "peak sensitivity [to mutagenic effects] is found in the most immature spermatids". This statement is in direct contradiction to the findings on recessive lethals quoted above. Presumably it is based on Dr. Bateman's own recent experiments with *Drosophila*[10]. In these experiments he measured dominant lethality by the percentage of non-hatching eggs and came to the conclusion that its incidence was highest in very early postmeiotic stages. But hatchability data which are not supported by cytological examination of the unhatched eggs are no unambiguous measure of rate of mutation and become utterly unreliable when the stage of oligospermy is approached. It is true that the X-ray dose to which Dr. Bateman exposed *Drosophila* males was too low to result in a stage of pronounced infertility; but it is probable that the very low hatchability on the ninth day after irradiation, which he interprets as entirely due to dominant lethality, was in fact partly caused by lack of sperm. It seems to me that Dr. Bateman's reasons for postulating a difference between the sensitivity patterns of mouse and *Drosophila* testis are not valid. It is true that, pending more precise information on the treated germ cell stages in the mouse, Dr. Bateman's data cannot be taken as definite proof that the sensitivity pattern is the same in both species; but even less can they be used as proof that the two patterns are different.

This question has a bearing on the assessment of radiation damage to the human testis. If Dr. Bateman's contention were correct, extrapolation would be impossible from *Drosophila* to man and very suspect from mouse to man. On the contrary, the observation that these two patterns show such a remarkable degree of parallelism suggests that we may be dealing with a fundamental property of male metazoon germ cells, and this may give us some confidence in extrapolations from animals to man.

C. AUERBACH

Institute of Animal Genetics,
Edinburgh.
Jan. 10.

[1] Bateman, A. J., *Nature*, **178**, 1278 (1956).
[2] Auerbach, C., *Z.i.A.V.*, **86**, 113 (1954).
[3] Khishin, A. F. E., *Z.i.A.V.*, **87**, 97 (1955).
[4] Lüning, K. G., *Hereditas*, **40**, 295 (1954).
[5] Muller, H. J., *et al.*, Nat. Res. Council Committee on Growth, 9th Ann. Rep., 113 (1955).
[6] Baker, W. K., and Halle, E. V., *Proc. U.S. Nat. Acad. Sci.*, **39**, 152 (1953).
[7] Nordback, K., and Auerbach, C., Brit. Emp. Cancer Camp. Report 395 (1955).
[8] Oakberg, E. F., *Radiation Res.*, **2**, 369 (1955).
[9] Friesen, H., *Biol. Zh.*, **6**, 1055 (1937).
[10] Bateman, J. A., *J. Genet.*, **54**, 400 (1956).

WE consider that Dr. Bateman's timing of spermatogenic events in the mouse[1] requires discussion because of the impact it bears on the interpretation of radiation sensitivities. We believe that his estimate of six to seven weeks between spermatocytes and ejaculation, based on genetical evidence, shows a serious discrepancy with other estimates