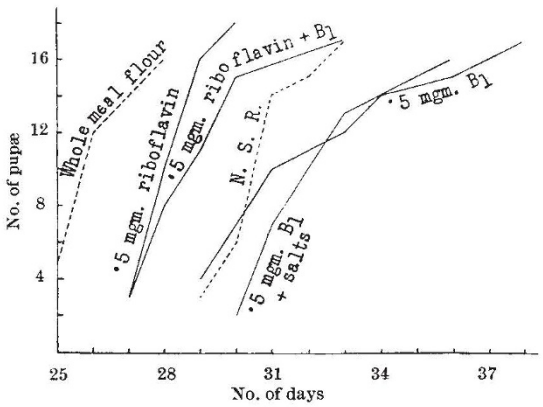

Fig. 3.

LARVAL GROWTH OF *Tribolium confusum* ON NATIONAL STRAIGHT RUN FLOUR (N.S.R.) AND ON N.S.R. SUPPLEMENTED BY VITAMIN B_1, RIBOFLAVIN AND SALTS. QUANTITIES PER 2 GM. OF FOOD.

Addition of pure vitamin B_1 (aneurin) to patent flour does not in the least alter its nutritional qualities; addition of riboflavin, however, to patent flour containing vitamin B_1 causes a very startling improvement (Fig. 2). We have found that very small quantities of riboflavin produce a marked effect (0·031 mgm. per 2 gm. of food). (Frobrich (1939)[7] has shown Tribolium to grow well on food containing only 0·008 mgm. of riboflavin in 1·5 gm. of food. Larger quantities were found to be toxic, but we cannot confirm this.) The apparent differences in the efficiency of diets containing different quantities of riboflavin are possibly not significant and may be due to insufficient mixing. Riboflavin was mixed with patent flour in the dry state, and the series was obtained by dilution with more patent flour. It appears, therefore, that most of the deficiency of patent flour is remedied by addition of riboflavin. In this dilution series with riboflavin the diets also contained vitamin B_1 (0·5 mgm. per 2 gm. of food). Later experiments proved, however, that the same favourable effect is produced without adding B_1.

Similar experiments with National straight run flour (N.S.R.) led to the same kind of results (Fig. 3). Although the nutritional qualities of N.S.R. for Tribolium are not much inferior to those of wholemeal flour, addition of riboflavin to N.S.R. produced a marked improvement. Adding B_1 to N.S.R. alone or to N.S.R. plus riboflavin caused the diets to be slightly less efficient, which, however, might not be significant.

An attempt was also made to find out whether any deficiency of salts in patent flour and N.S.R. could be demonstrated. Addition of MacCollum's salt mixture in the proportion of 1 per cent to patent flour and to N.S.R., however, showed no significant effect (Fig. 3).

The results obtained with Tribolium fully agree with those recently reported by H. Chick[1] on the white rat. In both cases the nutritive value of N.S.R., even when supplemented with vitamin B_1 and salts, is markedly inferior to that of wholemeal flour. Chick's suggestion that this may be partly due to deficiency in riboflavin has been proved to be correct. Most of this deficiency is corrected by adding riboflavin. Moreover, the efficiency of patent flour and N.S.R. both supplemented with riboflavin is almost identical, and the efficiency of supplemented patent flour is apparently greater than that of unsupplemented N.S.R. (Figs. 2 and 3). This proves that the nutritional difference, demonstrable with Tribolium, between the two kinds of white flour of 40 and 73 per cent extraction is almost entirely due to lack of riboflavin in patent flour.

No practical conclusion can be drawn from the fact that Tribolium does not need more B_1 than is present in patent flour. Since the deficiency of white flour in B_1 is well known and the need of Tribolium for B_1 has been demonstrated, the amount of B_1 in patent flour seems to be well above the threshold of the requirements of Tribolium. On the other hand, if one considers the very low requirements of Tribolium for riboflavin and the startling improvement in the nutritional qualities of white flour after adding riboflavin, the deficiency of patent flour and even straight run flour in riboflavin must be regarded as being serious. Supplementing white flour with vitamin B_1 would, therefore, leave the deficiency in riboflavin unremedied.

We wish to thank Dr. J. D. Mountfield, of the Research Association of British Flour Millers, for supplying samples of National straight run flour, patent flour and wheat germ.

[1] Chick, H., *Lancet*, Oct. 26 (1940).
[2] Willcox, W., *Food*, **10**, 147 (1941).
[3] Chapman, R. N., *J. Gen. Physiol.*, **6**, 565 (1924).
[4] Sweetman, M. B., and Palmer, L. S., *J. Biol. Chem.*, **77**, 33 (1928).
[5] Nelson, J. W., and Parker, L. S., *J. Agric. Res.*, **50**, 894 (1935).
[6] Street, H. R., and Palmer, L. S., *Proc. Soc. Exp. Biol. N.Y.*, **32**, 1500 (1928).
[7] Fröbrich, G., *Z. vergl. Physiol.*, **27**, 335–383 (1939).
[8] Offhaus, K., *Z. vergl. Physiol.*, **27**, 384–428 (1939).

FATIGUE FOLLOWING HIGHLY SKILLED WORK*

BY PROF. F. C. BARTLETT, F.R.S.

IF the character and causation of fatigue following highly skilled work are to be understood, the first need is for the discovery of more relevant and experimentally controlled facts. Unfortunately, almost all the investigators who have attempted to study fatigue of this type have adopted methods taken over with very slight change from those which have proved valuable in the study of simple muscular fatigue. They have chosen elementary operations usually considered to require some 'mental' effort—such as easy calculations, word or colour recognition and naming and the like—have repeated these operations over and over again for long periods, and have tried to express the resulting fatigue in terms of the diminution in quantity or quality of the work done.

The skill fatigue of daily life is not set up under such conditions. Routine repetition of simple actions

* Substance of the Ferrier Lecture of the Royal Society, delivered on May 29.

is not characteristic of any highly skilled work, and least of all of work having a strong 'mental' component. The operations involved here are marked by complex, co-ordinated and accurately *timed* activities. The stimuli in response to which these activities are set up are neither simple nor do they usually fall into an order of fixed succession. They have the character of a field, or a pattern, which has become very highly organized, and may retain its identity in spite of a great diversity of internal arrangement.

It is possible to develop fully controlled experimental situations in which these realistic considerations have full play. When this is done, the picture of fatigue following highly skilled work which emerges has certain strongly marked characters.

In such fatigue the 'standards' accepted and followed by the central nervous system unwittingly deteriorate. The operator tends to think that he is doing better work, because errors treated as significant all the time get wider and wider limits. Until a stage of great fatigue is reached, it is far more likely that the right actions will be performed at the wrong times than that the wrong actions will be performed. If accurate timing is insisted upon, gross mistakes of action may appear. The stimulus field splits up. Its pattern character alters. It becomes a collection of unconnected signals for action, with some of these predominant over all the others. Particularly stimuli which are in the margin of the pattern, not closely organized with the central field, are ignored, 'forgotten', and serious lapses of specific reactions occur. There is a marked change in the effect of certain 'distracting', or additional stimuli. Sensations of bodily origin, in particular, become more pressing and insistent, and affect the performance in ways peculiar to the tired operator.

Side by side with all these changes go constant subjective symptoms. Verbal reports about any circumstances connected with known failure of performance become increasingly inaccurate, and errors are regularly projected upon objective conditions, or attributed to the interference of other people. There is a tremendous growth of irritability.

The light thrown by this picture upon the relation of high-level central nervous functions to simpler neuro-muscular mechanisms was discussed.

ROLE OF RADIATION MUTATIONS IN MANKIND*

By Dr. H. J. Muller

ACCEPTING, on the basis of work with organisms in general, including mice, the conclusion that X-rays and other high-energy radiations produce gene mutations in any human germ cells that are exposed to them, with a frequency exactly proportional to the dose of radiation used, we may ask: What are the conditions governing the manifestation of these mutations? When attention is confined to the recessive gene-mutations, which appear as the most pronounced and constant, yet insidious, genetic effects, it may be approximately calculated how long the latent period would be between the time of exposure of an individual who afterwards reproduces and the appearance of some descendant manifesting a recessive mutation that had been produced in one of the former's germ cells.

For the manifestation of a recessive gene two germ cells having the same allelically acting recessive genes must come together, forming a homozygote—an event that would happen with almost negligible frequency in the first-generation offspring, even from two irradiated parents. There are, however, two ways in which a homozygote manifesting the mutated gene could eventually be formed. One is by a germ cell containing it meeting in fertilization another germ cell which chances to contain an identical or allelic recessive gene which, having originated by some independent mutation, was already present in the population in some parallel line of descent. The chance of this event depends upon the frequency of such recessive mutated genes in the general population, and this can be calculated if we know the so-called 'spontaneous' mutation frequency, the rate at which individuals manifesting such genes are being eliminated in competition with normals, and the amount of inbreeding in the population. Sufficient data exist for calculating that under the condition of random breeding—which would give the highest frequency of such genes—very few recessive genes the manifestation of which would be of seriously detrimental character would exist in frequencies exceeding 1 in 30 or, more probably, 100 germ cells, in the general population. Thus it would on the average require some 30 or, more likely, 100 or more generations of breeding—some 750–3,000 years of human history—before the mutated gene would manifest itself by this process.

The other way in which the gene could manifest itself would be by a germ cell containing it meeting another containing a relative, so to speak, of the same gene, that is, an identical gene derived from the same ancestral mutated gene of the original treated individual. This requires the breeding together of more or less related individuals—'inbreeding'—and the chance of its occurrence depends on the total amount of inbreeding occurring in the population. In determining the frequency of this effect a special method of calculation has been employed, utilizing a simple proportionate relation of 1 to 4 which I have calculated to hold between the frequency of two related genes thus meeting each other and the frequency of two individuals having the same name by reason of some near or distant relationship marrying each other. Reckoning from known statistics on the latter events, it can be shown that, even in rural English communities, the chance of a mutated gene manifesting itself by this process is only about 1 in 200. That is, it would on the average take about 200 generations, or at least 5,000 years, for the gene to attain manifestation in such manner. Both causes operating together would not suffice to give a period of less than 600 years, and more probably one of thousands of years.

Of course these periods are only averages for the time of first manifestation; actually, the first manifestations of the different mutated genes would be

* Substance of a paper read at the annual meeting during April 28–29 of the U.S. National Academy of Sciences.