outline of different insects which will be published in full elsewhere. A parallel study of the isolated waxes is being made in this laboratory by Mr. J. W. L. Beament.

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Repeated Doses of Drugs

THE following calculations, which deal with the theory of the accumulation of drugs in the body, involve two assumptions which are known to be justifiable in certain cases. The disappearance of the drug from the body is assumed exponential, and the time taken for absorption and distribution is neglected.

Let a series of equal doses (d) be given at equal intervals of time (t') in such a way that no dose is given at zero time and the first dose is given at time t' . Let the concentration produced in the body, or in the plasma, by one dose be d . Let the total concentration at time t be D , and let the drug disappear according to the formula $\frac{dD}{dt} = -kD$, or $D = D_0 e^{-kt}$. At the end of the second interval of time, $D = de^{-kt'}$, or dp , where $p = e^{-kt'}$. Immediately after the second dose, $D = d(1 + p)$, and immediately after the n th dose, $D_n = d(1 + p + p^2 + \dots + p^{n-1})$. The expression for the sum of this series gives $D_\infty = d/(1 - p)$. This expression can also be deduced from the fact that, when the curve ceases to rise, the effect of each dose (d) must exactly replace

the amount disappearing between doses [$D_\infty(1 - p)$]. Simple algebra gives the result

$$D_n/D_\infty = 1 - p^n = 1 - e^{-knt'} = 1 - e^{-kt}.$$

The maxima of the curve of accumulation therefore lie on a curve which is identical with the curve of the disappearance, but inverted. This is true whatever the dose and whatever the dose interval. The curve through the minima lies below the curve through the maxima at a constant distance corresponding to the size of a single dose. It is thus possible to predict the accumulation of a drug from a knowledge of its disappearance.

The time taken for a drug to accumulate in the body is often too slow for therapeutic requirements and is diminished by giving large doses in the early stages of treatment. It may be calculated that, if the dose, or the rate of dosing, is doubled, the time taken for the curve through the maxima to reach 90 per cent of its final value on single doses is reduced to about 26 per cent of the time which would be taken if single doses were used throughout. If the dose is quadrupled, the time is reduced to about 12 per cent, provided that the approximations mentioned above are still valid.

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Thermal Fatigue of Metals

WHEN small steel-backed bearings of tin- and lead-base alloys were repeatedly heated and cooled over the range 30°–150° C., marked cracking occurred throughout the tin-base alloy, but not in the lead-base alloy. Continuation of the cyclic process led ultimately to the disruption of the tin-base alloy. Since specimens of similar alloys unattached to a steel shell were found to behave in the same manner, it was thought that the metals forming the bases of the alloys were responsible for the difference in behaviour. For this reason, lead (99.99 per cent) and tin (99.9 per cent) were examined under the same conditions, the investigation being later extended to cadmium (99.97 per cent), zinc (99.97 per cent) and tellurium (B.D.H. Purity).

The specimens of lead, tin, cadmium and zinc were in the annealed state and all but lead were electrolytically polished. The lead specimens were prepared by careful polishing followed by etching with the usual acetic acid-hydrogen peroxide reagent. These methods were adopted to obtain surfaces for metallographic examination which were free from deformation. The specimens were then alternately heated and cooled over the range 30°–150° C. for a number of cycles. In the case of tin, cadmium and zinc, this treatment produced definite signs of plastic deformation, indicated in some cases by twinning and in others by slip lines. Photomicrographs illustrating the effect for cadmium are reproduced herewith. Close examination of lead specimens treated in the same manner failed to reveal any evidence of plastic deformation.

In the majority of cases, plastic deformation was observed even after one cycle, but it was limited to a few grains only. As the number of cycles was increased, signs of plastic deformation appeared in more grains and became more pronounced in individual grains until finally most grains were affected.

Curves of accumulation. Time for half-clearance = 24 hours; $1/k = 34.6$ hours; $t' = 4$ hours; $p = 0.891$. Lower curve— $d = 1$ gm.; $D_\infty = 9.2$ gm. Upper curve—first 6 doses = 2 gm.; $D_\infty = 13.4$ gm.