chain at C-17, is almost as effective an inhibitor. The effect of substitution at the 11-position depends upon the nature of the oxygen function. The presence of a ketone group at C-11, as in cortisone-21-succinate, does not decrease inhibitory activity as much as does a C_{11}-β-OH group, such as is present in hydrocortisone-21-succinate. Alteration in the A ring, either by formation of a derivative at C-3 [testosterone-3-O-(carboxymethyl)oxime] or by aromatization of the ring (estrone and estradiol), greatly decreases or abolishes inhibitory activity. It would appear, from these results, that the structural features of ring A, that portion of the hapten molecule which is furthest removed from the point of attachment to the BSA, determines, to a great extent, the specificity of the reaction between T-17-BSA and anti-T-17-BSA. It is expected that continuation of studies of this type, by use of additional soluble steroid derivatives, will reveal more precisely the chemical basis of specificity.

An interesting example of specificity is depicted in Fig. 1, in which the inhibiting effectiveness of T-17-succinate and C-21-succinate on the reactions of C-21-BSA and T-17-BSA with an antiserum to C-21-BSA are plotted. C-21-succinate, the homologous hapten, equally inhibits the reaction with the homologous antigen, C-21-BSA, and the heterologous antigen, T-17-BSA. On the other hand, the heterologous hapten, T-17-succinate, inhibits the cross-reaction with T-17-BSA much better than it inhibits the reaction with the homologous antigen, C-21-BSA. Thus, although anti-C-21-BSA cross-reacts with T-17-BSA, by addition of a suitable concentration of T-17-succinate it should be possible to inhibit practically completely the cross-reaction with negligible effect on the homologous reaction. It is hoped that, in this manner, the in vivo activity of anti-C-21-BSA may be studied without complicating cross-reactions, and such investigations are now in progress.

It has thus been demonstrated that several steroid hormones may act as haptens when coupled to a protein, and antibodies with steroid specificity may be elicited (*5*).

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17 September 1958

Vanguard Measurements Give Pear-Shaped Component of Earth's Figure

The determination of the orbit of the Vanguard satellite, 1958β_2, has revealed the existence of periodic variations in the eccentricity of that satellite (*1*). Our calculations indicate that the periodic changes in eccentricity can be explained by the presence of a third zonal harmonic in the earth's gravitational field. The third zonal harmonic modifies the geoid toward the shape of a pear. In the present case, the stem of the pear is up—that is, at the North Pole. According to our analysis, the amplitude of the third zonal harmonic is 0.0047 cm/sec² in the surface acceleration of gravity, or 15 meters of undulation in the geoid.

Figure 1 shows the observed variation in eccentricity. The period of the variation in eccentricity is 80 days, approximately equal to the period of revolution of the lines of apsides. The eccentricity is a maximum when the perigee is in the Northern Hemisphere. The amplitude of the variation is 0.00042 ± 0.00003. Similar perturbations may exist in the angle of inclination of the orbit, although the data for them are much less accurate. No perturbations of this magnitude appear to exist in the semimajor axis.

In principle, the perturbation might be caused by both odd and even harmonics. However, the even harmonics can be excluded because the observed effect has opposite signs in the Northern and Southern hemispheres. Furthermore, we can also exclude tesseral harmonics (those which depend on longitude as well as latitude) because these also are the same in the Northern and Southern hemispheres, apart from a shift in longitude. We are left with the zonal harmonics (those which depend only on latitude) of odd degree.

Of the odd zonal harmonics, the first degree is forbidden; and those of higher degree are unlikely to have a large effect because they die out inversely as the $(n+1)$ power of the distance. The effect is therefore due mostly to the third zonal harmonic, with a possible contribution from the fifth.

Accordingly, a calculation was made of the effect of the third zonal harmonic on the orbit elements of 1958β_2, by methods developed by O'Keefe and Batchlor (*2*). In the resultant expression for the eccentricity, the dominant terms were those whose argument was the mean motion of perigee. These were larger than the others by a factor of 10^3. Keeping only the large terms, we find

$$e = e_0 + \frac{3}{2} A_{3,0} \frac{(1-e^2)^{1/2}}{na^6} \frac{1}{n'} \times \sin i \left(1 - \frac{5}{4}\sin^2 i\right) \sin \omega \qquad (1)$$

where $A_{3,0}$ represents the coefficient of the third zonal harmonic in the notation of Jeffreys (*3*), n is the orbital mean motion and n' is the mean motion of the perigee, e is the eccentricity and e_0 the mean eccentricity, i is the angle of inclination, ω is the argument of perigee, and a is the semimajor axis.

Setting in the constants of the orbit and the observed amplitude of e, we find

$$A_{3,0} = (2.5 \pm 0.2) \times 10^{29} \qquad (2a)$$

in meter-second units. Utilizing the relation given by Jeffreys,

$$A_{n,s} = \frac{c^{n+2}}{n-1} g_{n,s}$$

(where $A_{n,s}$ is the coefficient of the disturbing potential, $g_{n,s}$ is the acceleration of gravity at the surface of the earth, and c is the earth's equatorial radius), we find that the third zonal harmonic of gravity at the earth's surface, in milligals, is

$$g_{3,0} = 4.7 \pm 0.4 \qquad (2b)$$

Equation 2 is relevant to what Vening Meinesz (*4*) and Heiskanen call the "basic hypothesis of geodesy." These authors assume that the earth's gravitational field is very nearly that of a fluid in equilibrium. They consider that the deviations from such an ellipsoid, in any given area, do not exceed about 30 milligal-megameter units—that is, they assume that one will not find deviations of more than 30 milligals over an area of 1000 kilometers on a side, or deviations of more than 3 milligals in an area 3000 kilometers on a side.

Our determination of the third-degree zonal harmonic shows that the hypothesis of Vening Meinesz and Heiskanen is

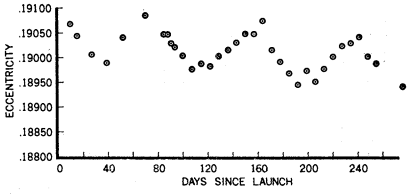

Fig. 1. Eccentricity of satellite 1958β_2 (Vanguard).

not justified; for example, each of the polar areas has a value of about 120 milligal-megameters, and each of the equatorial belts a value more than twice as great.

The presence of a third harmonic of the amplitude (*2*) indicates a very substantial load on the surface of the earth. Following the arguments of Jeffreys, we may calculate the values of this load and the minimum stress required in the interior to support it. We find a crustal load of 2×10^7 dy/cm^2. We can choose between assuming that stresses of approximately this order of magnitude exist down to the core of the earth, or that stresses of about 4 times that amount exist in the uppermost 700 kilometers only (*3*, p. 199). These stresses must be supported either by a mechanical strength larger than that usually assumed for the interior of the earth or by large-scale convection currents in the mantle (*5*).

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Synchronized Cell Division and DNA Synthesis in a Lactobacillus Acidophilus Mutant

Abstract. Withdrawal and subsequent restoration of deoxyriboside to a deoxyriboside-requiring mutant leads to synchronous cell division. There is a time lag between restoration and the first synchronous division; during this time the amount of deoxyribonucleic acid (DNA) per cell increases in stepwise fashion, and mass per cell increases linearly with time. The onset of cell division is heralded by cessation of DNA synthesis and an abrupt increase in rate of mass synthesis.

The intracellular events leading to cell division are under intensive study currently, and many approaches have been employed. One of the most promising methods is the induction of synchronized division in a population whose members normally divide randomly in time. Synchronization has been accomplished by means of temperature shifts (*1*), fractionation of cell popoulations (*2*), and addition of thymine to a thymineless *Escherichia coli* mutant (*3*). All methods are subject to the objection that the process of induction may produce abnormal divisions, and that the biochemical events preceding these divisions may have no relation to those preceding normal divisions. This objection can be overcome partly by comparison of results from as many methods of synchronization as possible and by use of a method which has specific and reasonably predictable biochemical effects.

The method described here (*4*) employs a mutant with a block at the deoxyriboside level of DNA synthesis, and synchronization is accomplished by withholding deoxyriboside from otherwise normally nourished cells and subsequently restoring it. The direct effect of this method is specific inhibition of DNA synthesis; the indirect effect of inhibition of DNA synthesis is small during the period of abnormal nutrition, as judged by high viability and continuing growth in the present instance. Ribonucleic acid synthesis continues in the absence of DNA synthesis (*5*). A major indirect effect is, of course, inhibition of cell division.

The mutant strain employed in these studies was *Lactobacillus acidophilus* R26. This strain grows in synthetic medium and has a specific requirement for deoxyriboside or deoxyribotide. Hoff-Jorgensen (*6*) has used this mutant for quantitative bioassay of DNA. The synthetic medium (LSM) was the same as Hoff-Jorgensen's, but with the addition of 10 mg of uracil and 0.5 mg of pyridoxine per liter, as suggested by Siedler *et al.* (*7*). Thymidine was used to satisfy the deoxyriboside requirement. Where indicated, thymidine was supplied at a concentration of $3 \times 10^{-6} M$, an amount just sufficient to give maximum growth.

For the majority of experiments, cells were prepared by growing them for 16 hours in LSM with thymidine. These cells were harvested, washed, and suspended at about 10^7 cells per milliliter in synthetic medium lacking thymidine. The suspension was stirred at 37°C, and aliquots were withdrawn for viable cell counts and turbidity and DNA determinations. Viable cell counts were made by the indirect method; suitably diluted aliquots were plated on nutrient agar, and the number of viable cells per milliliter was determined from colony counts. Turbidity measurements provide a direct estimate of cell mass rather than of number of cells (*8*). Turbidity (optical density at 500 mμ in the range of 0 to 0.4) was found experimentally to be proportional to cell protein per milliliter (determined by the Folin phenol method), irrespective of cell size. This is important because the cells elongate during thymidine starvation and break up into smaller units when division starts. De-

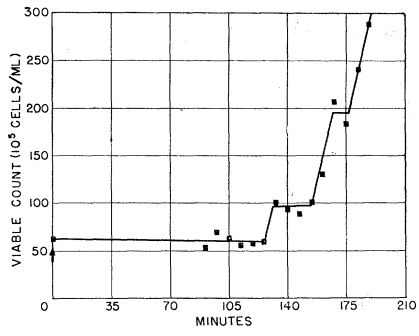

Fig. 1. Synchronous cell division. The time of addition of thymidine is indicated by the arrow.

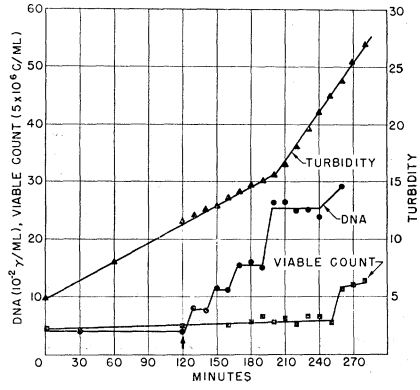

Fig. 2. Variation of DNA, turbidity, and viable cell count with time in a synchronized culture. Incubation in the absence of thymidine started at time 0; addition of thymidine is indicated by the arrow.

oxyribonucleic acid determinations were made by the Ceriotti method as modified by Keck (*9*). Cells were washed twice in cold 5-percent trichloroacetic acid and extracted in hot trichloroacetic acid, and the extract was analyzed for DNA.

Figure 1 shows two cycles of synchronous division. The cells were incubated in the absence of thymidine for 3 hours, then thymidine was added, at time 0 in the figure. There is a lag of about 2 hours before the first division. Two or three synchronous divisions follow the lag in rapid succession, the later ones being less distinct than the earlier. One synchronous division cycle takes about 30 minutes, which is much less than the 1½-hour generation time of nonsynchronous log phase cells.

Viability as a function of time during the course of starvation for thymidine has been determined, but the curve is omitted here for brevity. Death, presumably due to "unbalanced growth" (*3*), begins to appear only after 5 or 6 hours' starvation, if excessive aeration is avoided.

Figure 2 shows the results of simultaneous determinations of DNA, turbidity, and viable cell count. There is no net synthesis of DNA in the absence of