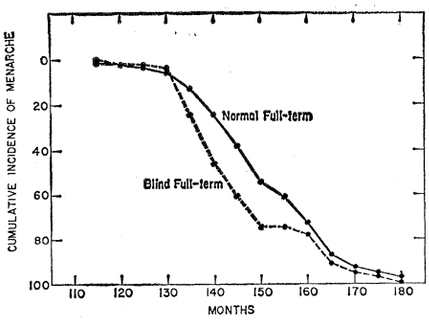

Fig. 2. Cumulative incidence of menarche (expressed as percentage of total) of full-term groups: blind and normal.

a delay in sexual maturation, and then a decrease in the proportion of time spent in vaginal estrus. For several weeks after bilateral orbital enucleation, rats show a marked decrease in vaginal estrus (that is, decrease in the incidence of estrous phases as observed in daily vaginal smears); after 3 or 4 weeks, when normal cycling starts again, the cycles are not affected by environmental illumination (*12*).

In view of the results of these experiments with animals, it is surprising that in this preliminary study early blindness in humans appears to accelerate sexual maturation. Moreover, the magnitude of the effect appears to be related to the severity of the visual loss.

One might postulate either that light affects rat and human gonads differently, or that loss of visual function, even when it includes loss of light perception, does not produce the same neuroendocrine effects as the actual absence of light. (This consideration arises in our study, in which we have substituted blindness for absence of light.) It has recently been shown that environmental light can penetrate the mammalian skull in sufficient amount to activate photoelectric cells imbedded in the brain tissue (*13*). It is therefore a possibility that light, acting on the neuroendocrine axis of the blind human (even one who is totally without light perception) in the absence of retinal responses to light, produces an imbalance which results in earlier menarche. However, at least one effect of light on the human endocrine apparatus seems to require receptors which are located solely in the retina, since the ability of light to induce a rapid eosinopenia (presumably through the release of adrenal steroids) is lost in the presence of macular degeneration (*14*).

It is well known that emotional factors can influence ovulation in humans, and that a wide variety of diseases, ranging from simple malnutrition (*15*) to specific endocrinopathies, depress ovarian function. It might be conjectured that the relation between blindness and human ovary function is nonspecific, and a consequence of the emotional stress and behavioral adaptations associated with blindness. This hypothesis seems unlikely: although there are many instances of nonspecific inhibition or delay of human gonad function, few if any are known in which acceleration occurs without some specific disturbance in neuroendocrine function [for example, hypothalamic and pineal tumors (*16*)]. It seems more probable that stimulation of the retina by environmental light produces a specific effect on the human ovary.

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References and Notes

1. E. Scharrer and B. Scharrer, *Neuroendocrinology* (Columbia Univ. Press, New York, 1963), pp. 51–56.
2. J. D. Green, *Textbook of Endocrinology*, R. H. Williams, Ed. (Saunders, Philadelphia, 1962), p. 885.
3. We thank the following institutions for their cooperation: the Boston Lying-in Hospital; the Schools of Nursing of the Beth Israel Hospital, Boston, the Children's Hospital Medical Center, Boston, and the Massachusetts General Hospital, Boston; the Arizona State School for the Deaf and Blind, the Arkansas School for the Blind, the California School for the Blind, the Colorado School for the Deaf and Blind, the Diamond Head School, Honolulu, the Iowa Braille and Sight-Saving School, the Kansas School for the Blind, the Nebraska School for the Blind, the New York State School for the Blind, the Ohio State School for the Blind, the Oregon State School for the Blind, the Tennessee School for the Blind, and the Virginia State School.
4. This group of 181 females was composed of 22 girls born between 1938 and 1949 at the Boston Lying-in Hospital, 14 girls in M. J. Kings RLF series [*Arch. Ophthalmol.* **43**, 694 (1950)] born for the most part in New England between 1938 and 1949, and 145 girls born between 1939 and 1954, who were or had been pupils in the various schools for the blind listed in reference (*3*).
5. Girls who were born at the Boston Lying-in Hospital between 1938 and 1949.
6. Girls who were or had been pupils at the schools for the blind mentioned in reference (*3*) born between 1938 and 1954. Of more than 150 girls whose records were examined, only 54 were judged admissible to the study, by criteria already given.
7. Girls born between 1940 and 1946 who were, at the time of the study, students in the nursing schools of three Boston hospitals: 63 at the Massachusetts General Hospital, 75 at the Beth Israel Hospital, and 98 at the Children's Hospital.
8. T. L. Terry, *Am. J. Ophthalmol.* **25**, 203 (1942); V. E. Kinsey and L. Zacharias, *J. Am. Med. Soc.* **139**, 139 (1949); L. Zacharias, *Am. J. Ophthalmol.* **35**, 1426 (1952); A. Patz, L. E. Hoeck, E. De La Cruz, *ibid.*, p. 1248; V. E. Kinsey, *A.M.A. Arch. Ophthalmol.* **56**, 481 (1956); L. Zacharias, *Pediatrics* **25**, 726 (1960).
9. We thank Mindel C. Sheps, Department of Biostatistics, University of Pittsburgh Graduate School of Public Health, for her valuable assistance in setting up the life tables and reviewing this manuscript; M. Merrell, L. E. Shulman, *J. Chronic Diseases* **1**, 12 (1955).
10. V. Critchlow, in *Advances in Neuroendocrinology*, A. V. Nalbandov, Ed. (University of Illinois Press, Urbana, 1963), pp. 377–402.
11. V. M. Fiske, *Endocrinology* **29**, 187 (1941).
12. R. J. Wurtman, E. W. Chu, J. Axelrod, unpublished observations.
13. W. F. Ganong, M. D. Shepherd, J. R. Wall, E. E. Van Brunt, M. T. Clegg, *Endocrinology* **72**, 962 (1963).
14. M. Radnot, E. Wallner, M. Hönig, *Acta Biol. Acad. Sci. Hung.* **Suppl. 4**, 47 (abstract) (1962).
15. R. F. Fletcher and P. S. Brown, *Clin. Sci.* **18**, 367 (1959).
16. H. G. Bauer, *J. Nervous Mental Disease* **128**, 323 (1959); J. I. Kitay, *J. Clin. Endocrinol. Metab.* **14**, 622 (1954).
17. This investigation was supported in part by PHS research grant NB-00640-10, from the Institute of Neurological Diseases and Blindness.

31 March 1964

Calcium Absorption in Man: Based on Large Volume Liquid Scintillation Counter Studies

Abstract. *A technique has been developed for the in vivo measurement of absorption of calcium in man after oral administration of 1 to 5 microcuries of calcium-47 and continuous counting of the radiation in the subject's arm with a large volume liquid scintillation counter. The maximum value for the arm counting technique is proportional to the absorption of tracer as measured by direct stool analysis. The rate of uptake by the arm is lower in subjects with either the malabsorption syndrome or hypoparathyroidism. The administration of vitamin D increases both the absorption rate and the maximum amount of calcium absorbed.*

Recent studies have shown that two significant physiologic mechanisms underlying the development of osteoporosis are (i) increased bone resorption (*1, 2*) and (ii) relative calcium deficiency (*1, 3*). Calcium deficiency may be a result of inadequate dietary intake or defective absorption of calcium. Among the techniques for the study of calcium absorption in man are meta-

Table 1. Calcium absorption calculated as the fraction of the dose absorbed in three subjects, one normal and two with symptoms of calcium malabsorption.

Subject	F.D. $= A - Be^{-k_1 t} + Ce^{-k_2 t}$					Percent absorption*
	A	B	C	k_1	k_2	
H.G.	.0082	.0091	†	.0133	†	58.7
H.G.	.0083	.0090	†	.0127	†	66.5
A.J.	.0009	.0011	.0034	.0133	.0069	0.0
G.S.	.0016	.0046	.0100	.0144	.0115	26.5
G.S.	.0041	.0045	†	.0093	†	

* Calculated from fecal excretion of Ca^{47} over 6-day stool collection period. † Shape of curve gave the best equation without introducing these terms.

bolic balances (*2, 3*), indirect isotopic procedures based on intravenous administration of tracers (*1, 2, 4*), and direct isotopic techniques based on measurement of the excretion of an orally administered dose (*5*) or measurement of the blood level at a single time point (*6*). Studies of metabolic balance and direct isotopic absorption based on information derived from pooled samples yield results that are averages of absorption over a period of several days. Indirect isotopic procedures calculate calcium absorption from steady-state, specific-activity measurements in blood, urine, and excretions in pooled stool collections, also yielding average values. None of these techniques permit examination of dynamic, short-term absorption mechanisms involved in the transit of calcium from the gastrointestinal tract to bone.

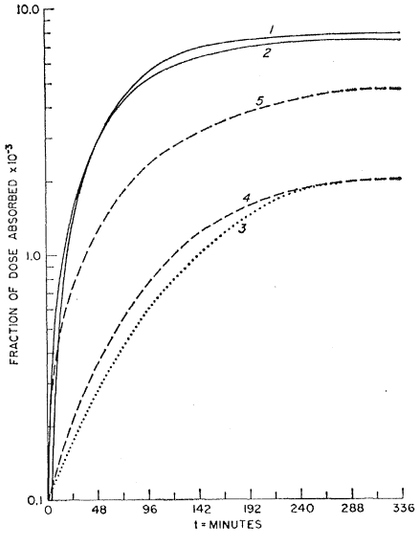

Fig. 1. Calcium absorption from arm count data plotted as the logarithm of the fraction of the administered dose against time. See text for details. Curve *1*, H.G., normal control; *2*, H.G., duplicate study; *3*, A.J., malabsorption; *4*, G.S., hypoparathyroid, basal study; *5*, G.S., with 10,000 units of vitamin D per day.

This report describes a simple, rapid procedure which may provide direct information on the mechanisms of calcium absorption. The development of large volume liquid scintillation counters (*7*) permits accurate estimation of very small amounts of γ-emitting isotopes in the arm or leg of a subject. After an oral dose of Ca^{47}, the radioactivity measured in a limb at any time thereafter would be the amount of the tracer that had been absorbed and transported to the blood, skin, muscle, and bone. It has been shown (*6*) that after maximal isotope absorption has occurred there is little change in blood radioactivity for several hours and skin and muscle retain only small amounts of radioactivity. The major fraction of tracer found in the arm would be that accumulated by the bone in the processes of exchange and accretion, and would serve not only as an index of the rate of transport from the intestine to the calcium-retaining sites in the bone, but also as a measure of calcium retention by that portion of the skeleton.

In our experiments the subject is seated or lies supine before the opening of an Armac scintillation detector (*8*) so that his forearm, extended sideways at the approximate level of his shoulder, is within the sensitive volume of the machine and the remainder of his body is out of direct line of vision of the port of the instrument. A lead apron is draped over the subject to further reduce the emission to the instrument from the chest and abdomen. Two hours after a meal the subject is given an oral dose of 1 to 5 μc of high specific activity Ca^{47} (from Oak Ridge National Laboratories) mixed with 100 ml of milk (approximately 100 mg of calcium). The container is rinsed three times with distilled water and the rinsings swallowed. The count rate of the arm is measured at 10-minute intervals, interspersed with counts of the background obtained with the subject in the same position but with his arm at his side, out of the sensitive well. In most instances blood samples were obtained periodically from the opposite arm, confirming the low levels (less than 0.05 $\mu\mu$c/ml) of circulating radioactivity. Arm counting was continued for 6 hours and additional measurements were taken at intervals for 6 to 10 days after the tracer was administered. All stool and urine samples were counted for 5 days after the study was started. The data for the counts obtained from the arm were plotted, as shown in Fig. 1, as the logarithm of the fraction of the administered dose against time. These curves illustrate the general pattern obtained from different subjects, and show the fraction of dose absorbed into the arm as determined at 5- to 10-minute intervals. The resulting curve shows three components: (i) a rapid rise; (ii) a somewhat slower, but still rapid, rise; and (iii) a slowly increasing asymptotic portion. After 24 to 48 hours, the curve became horizontal or fell gradually. The curves were analyzed mathematically to arrive at an empiric exponential expression.

The fraction of dose absorbed into the arm (F.D.) is $A - Be^{-k_1 t} + Ce^{-k_2 t}$ (*9*). The constants and exponents for the equation, calculated for a preliminary series of studies, are summarized in Table 1.

Figure 1 shows the reproducibility of the data obtained by this technique. Two studies of a normal male control (H.G.) (curves 1 and 2), 1 month apart, yielded results that were almost superimposable. In contrast with these, the data in curve 3 were obtained from a subject (A.J.) with definite symptoms of calcium malabsorption, but without radiologic evidence of bone disease. It can be seen from these curves and from the data in Table 1 that, not only was the amount of radioactivity absorbed in this subject less than in the normal subject, but the kinetics of transport of calcium involved in attaining this maximum differed from those seen in H.G. The data from the studies on G.S., a subject with untreated idiopathic hypoparathyroidism, before (curve 4) and during (curve 5) oral administration of 10,000 units of vitamin D, indicated a possible absorptive defect for calcium in this disease and demonstrated that vitamin D increased both the rate of absorption and the amount of isotope deposited in bone.

Comparison of the values for A, the asymptotic maximum calculated for the arm counts, with the gross absorption measured from stool excretion of tracer, demonstrated excellent correlation.

Although this technique of arm counting does not yield values for absolute absorption of calcium, it does permit comparisons of relative absorption in the same subject before and during administration of substances affecting absorption, as well as comparisons between individuals with disturbances of mineral metabolism. Results are obtained within a few hours and no blood sampling or urine or stool collections are necessary. The amount of isotope required for accurate results is small, which permits studies to be carried out in children as well as in adults and allows repetitive studies in the same individual under different conditions of diet and drug therapy. The technical procedures are simple and rapid, and suggest that the technique may be of value in large-scale population studies of calcium absorption and survey protocols. Of greatest interest is that the in vivo procedure yields data describing the kinetics of the initial phase of transfer of calcium from the gastrointestinal tract to the bone and the modification of this phase by disease, diet, and pharmacologic agents.

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References and Notes

1. L. Lutwak and G. D. Whedon, *Federation Proc.* **22**, 553 (1963).
2. R. P. Heaney, *Am. J. Med.* **33**, 188 (1962).
3. G. D. Whedon, *Federation Proc.* **18**, 1112 (1959); B. E. C. Nordin, *Lancet* **1961-I**, 1011 (1961).
4. R. P. Heaney and G. D. Whedon, *J. Clin. Endocrinol. Metab.* **18**, 1246 (1958); W. J. Visek, R. A. Monroe, E. W. Swanson, C. L. Comar, *J. Nutr.* **50**, 23 (1953); M. Blau, H. Spencer, J. Swernov, J. Greenberg, D. Laszlo, *ibid.* **61**, 507 (1957).
5. M. Blau, H. Spencer, J. Swernov, D. Laszlo, *Science* **120**, 1029 (1954); C. L. Comar, R. A. Monroe, W. J. Visek, S. L. Hansard, *J. Nutr.* **50**, 459 (1953).
6. S. D. Bhandarkar, M. M. Bluhm, M. MacGregor, B. E. C. Nordin, *Brit. Med. J.* **1961-II**, 1539 (1961).
7. C. C. Lushbaugh, D. B. Hale, R. McGill, *Los Alamos Scientific Lab Report LAMS-2455 (1960)*, p. 223; C. C. Lushbaugh, *Nature* **198**, 862 (1963).
8. Packard Instrument Co., LaGrange, Illinois.
9. M. Berman, M. F. Weiss, E. Shahn, *Biophys. J.* **2**, 275 (1962).

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10 January 1964

Scaling of Apparent Viscosity

Abstract. *Observers made numerical judgments of the apparent viscosities of silicone liquids whose absolute viscosities ranged from 10.3 to 95,000 centipoises. Judgments were made by three procedures: shaking or turning a bottle containing the liquid, stirring the liquid with a rod with the eyes blindfolded, and stirring with the eyes open. For all these methods of judging, apparent viscosity was found to grow as the absolute viscosity raised to a fractional power. The exponents ranged from 0.42 to 0.46. The perception of viscosity follows the psychophysical power law that seems to govern prothetic perceptual continua.*

Judgments of relative viscosity, which can be made by tactual-kinesthetic or by purely visual means, have practical application in parts of the food industry (*1*), but they are also of interest in their own right. The purpose of the experiments reported herein was to determine how quantitative judgments of apparent viscosity depend on physical viscosity, as ordinarily defined, and to see whether this perceptual continuum follows the psychophysical power law that governs the growth of apparent magnitude on prothetic continua (*2*).

Procedure. The stimuli were seven blends of clear silicone fluid having viscosities 10.3, 95, 920, 12,500, 29,000, 61,000, and 95,000 centipoises (*3*). Approximately 150 ml of each fluid was placed in a clear, screw-cap, glass jar whose capacity was about 300 ml. These cylindrical glass jars were 7 cm in diameter and 9 cm high.

In each of three experiments a group of ten observers made two judgments of each stimulus. The stimuli were presented twice in a different irregular order to each observer. Written instructions were given. Those for the first experiment read as follows.

"I will give you a series of containers filled with liquids that vary in viscosity (internal friction). Shake each container and judge how viscous the liquid seems to be by assigning a number to it. Call the apparent viscosity of the first liquid any number that seems to you appropriate. Assign to the succeeding liquids numbers proportional to their viscosity. For example, if a liquid seems five times as viscous, assign a number five times as large as the first. If it appears to you 1/10 as viscous, assign a number 1/10 as large, and so on."

In the second experiment we employed a different group of 10 observers. This time the observers were blindfolded and instructed to stir the liquid with a round plastic rod (22 by 0.6 cm), making three turns to the right and three to the left.

The third experiment was the same as the second, except that the observers watched the liquid while they stirred it. Ten observers were used, six of whom had served in one or the other of the two previous experiments.

In all experiments the first stimulus presented was selected irregularly, except that neither of the two extreme stimuli was ever presented first.

Results. The twenty magnitude estimations of each stimulus in each experiment were used to compute a median and a geometric mean. The agreement generally obtained between these two measures suggests that magnitude estimations give distributions whose skewness can be corrected by taking logarithms. The geometric means of the data, of which both coordinates are logarithmic, are plotted in Fig. 1.

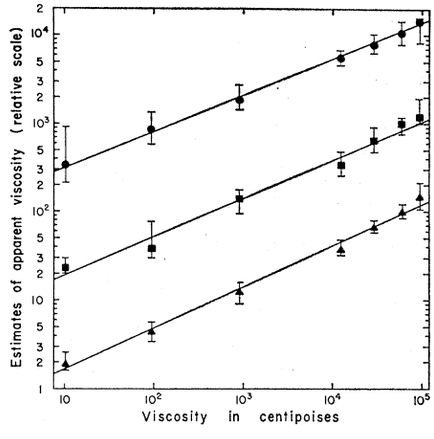

Fig. 1. Each point represents the geometric mean of 20 numerical judgments of apparent viscosity, two judgments by each of ten observers. Each power function represents a separate experiment. Circles: The observer watched the liquid while shaking or turning its container. Squares: The observers stirred the liquid while blindfolded. Triangles: The observers watched the liquid while stirring it. For clarity, the functions are separated vertically by one log unit. The exponents (slopes) are 0.42, 0.43, and 0.46. The vertical bars represent the interquartile ranges of the 20 judgments of each stimulus.