linear rise or an abrupt step, the beam was increased by 75 percent. There was also an increase of about 100 percent if the voltage on the inflector electrode was removed immediately after injection.

The largest beam with the bevatron aperture set at 6 in. × 18 in. was 3.5×10^{-11} coulombs per pulse (or about 2×10^{8} protons per pulse). The injected beam measured at the end of the inflector electrodes was 10^{-8} coulombs. The over-all particle efficiency of the machine then was about $\frac{1}{3}$ percent. In the full-scale bevatron the losses due to gas scattering should be negligible because of the higher injection energy. In addition, while the tank height is scaled up by a factor of four the size of the inflector electrodes need not go up at all, so that ions will have a greater chance of missing the inflector after injection. It is therefore reasonable to expect a particle efficiency of at least several percent in the full-scale bevatron.

The bevatron development at the Radiation Laboratory is sponsored by the Atomic Energy Commission. It is under the direction of E. O. Lawrence and involves the work of many people. W. M. Brobeck is responsible for the basic design. Major responsibilities are also carried by those listed as authors in references *4, 5, 8,* and *9.* R. S. Shankland, of the Case Institute, and F. H. Schmidt, of the University of Washington, carried out some of the experimental measurements on the $\frac{1}{4}$-scale model.

References

1. Brobeck, W. M. *Rev. sci. Instr.,* 1948, **19**, 545.
2. Crane, H. R. *Phys. Rev.,* 1946, **69**, 542.
3. Gooden, J. S., Jensen, H. H., and Symonds, J. L. *Proc. phys. Soc.,* 1947, **59**, 677.
4. Kerns, Q. A. *et al. Bull. Amer. phys. Soc.,* 1949, **24**, 8.
5. Lofgren, E. *et al. Bull. Amer. phys. Soc.,* 1949, **24**, 8.
6. McMillan, E. M. *Phys. Rev.,* 1945, **68**, 143.
7. Oliphant, M. L., Gooden, J. S., and Hide, G. S. *Proc. phys. Soc.,* 1947, **59**, 666.
8. Sewell, D. C. *et al. Bull. Amer. phys. Soc.,* 1949, **24**,
9. Smith, Lloyd, Garren, A. A., and Henrich, L. R. *Bull. Amer. phys. Soc.,* 1949, **24**, 8.
10. Twiss, R. Q. and Frank, N. H. *Rev. sci. Instr.,* 1949, **20**, 1.
11. Veksler, V. *J. Phys. U.S.S.R.,* 1945, **9**, 153.

The Comparative Biochemistry of Vitamin Function

Ernest Beerstecher, Jr.

The Biochemical Institute of The University of Texas and
The Clayton Foundation for Research, Austin

PLANNED STUDIES of comparative biochemistry and comparative physiology are few as compared with the voluminous data on comparative morphology. The trend of recent years in the biological sciences away from the descriptive and toward the functional viewpoint, however, has evoked increased interest and study of the comparative approach. This has for the most part centered around the more gross aspects of nutrition and metabolism. Simultaneously, there has been an increased appreciation of the values to be gained from the study of some particular functional entity throughout a range of species, such that comparative biochemistry may well dominate the next developmental phase of biological science.

The history of the discovery of vitamins and elucidation of the vitamin concept has drawn heavily upon interspecies relationships. Williams' (*6*) discovery in 1919 that the antiberiberi substance was probably identical with a microbiological growth factor opened up a point of view that has permitted rapid exploitation of the vitamin field. Parallel studies in highly dissimilar species have characterized much of the work with the B vitamins from their discovery until the very present (*3, 4*), and indeed this group is characterized by the ubiquitous biological nature of its occurrence (*11*). Consequently, there exists in the literature a large amount of data of such a nature as to render much of it suitable for examination from the comparative approach. It therefore seems timely to consider what principles may be derived from a consideration of these data.

Chemical structure, natural distribution, and physiological activity of the vitamins. A variety of factors tends to strengthen the validity of grouping the vitamins into three categories: the B vitamins, the fat-soluble vitamins, and vitamin C.

The B vitamins are characterized by a ubiquitous biological distribution, and have a wide variety of structures. Naturally occurring analogues essentially involve modifications only in functional groups. Other vitamins, are not ubiquitous, and if vitamin C is excluded, those remaining—vitamins A, D, E, and K—are seen to share the common properties of being structurally related to isoprene polymers. Their homologues have carbon chain modifications, and have a high species specificity in biological activity and occurrence (*10*). Among the higher species in which these vitamins are active, B vitamin homologues generally have little or no species specificity in activity. They do show a species specificity in distribution in a broad sense, pyridoxine and niacin predominating in the plant kingdom, and pyridoxal, pyridoxamine, and nicotinamide predominating in animals. B vitamin homologues frequently manifest great differences in biological activity among bacterial species.

The vitamin requirements of various animal species. Early in the study of vitamin B_1 it was pointed out that the vitamin B_1 requirement on a weight basis was larger for smaller animals (*2*), and this fact was easily associable with the fact that smaller animals have a higher basal metabolic rate (*1*). The species size relationship to metabolic rate is the observation upon which much of the present knowledge of comparative biochemistry is based, and it might logically be expected that more vitamin B_1 would be required to lubricate the more highly geared machinery of smaller species. Despite the importance of this relationship, no apparent effort has ever been made to apply it to the other vitamins until quite recently, when it was shown that the same relationship seems to hold, as far as existing data permit its assessment, for the other B vitamins (*9*). As in all such relationships, apparent species exceptions occur, but these are never such as to invalidate the general trend. By contrast, it has been recognized for some time that the vitamin A requirement is approximately the same on a weight basis for all species studied (*5*), and the limited data available on the requirements for vitamins C, D, E, and K suggest strongly that a similar consideration holds for them. These facts seem to indicate that, whereas the B vitamins function in fundamental roles in metabolism, as we now know that they do in most cases, the other vitamins have specialized functions not critically related to the basal metabolism. This conclusion is strongly supported by the apparent absence of these other vitamins from most microbial forms. The classification of both groups of substances under the single generic term of *vitamin* may frequently be misleading, because of the implication that they constitute a single fundamental functional group. From the purely biochemical standpoint, the groups have little or nothing in common.

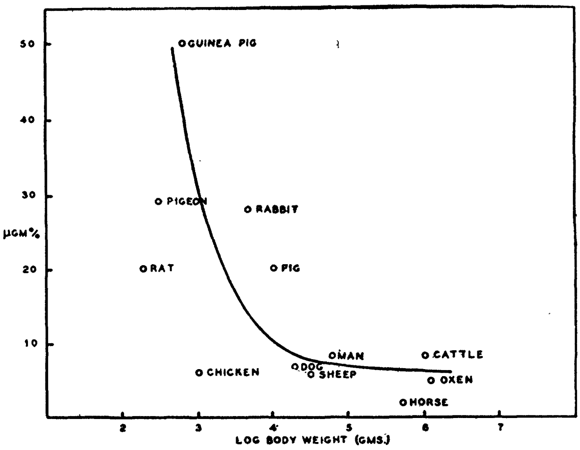

FIG. 1. Total thiamine in blood.

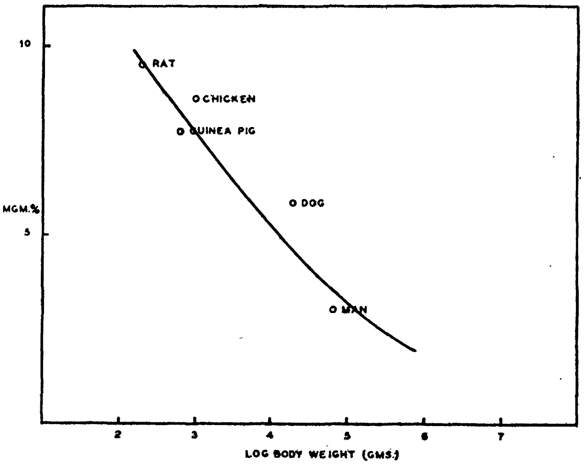

FIG. 2. Coenzyme I in blood.

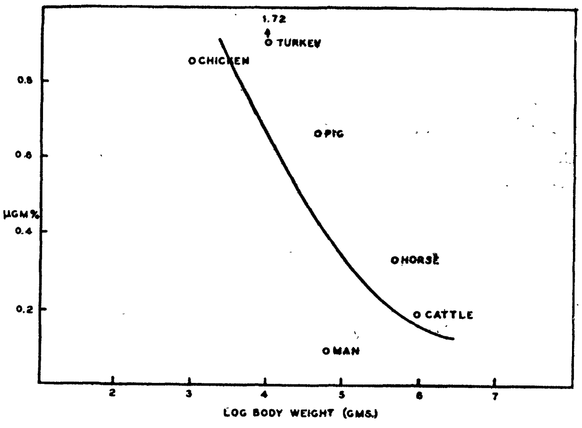

FIG. 3. Free folic acid in blood.

Blood levels of vitamins in various species. At high levels of vitamin intake, the blood level seems to indicate little more than the differential between the rate at which the vitamin enters the blood and the rate at which it leaves via excretory channels. At more moderate dietary levels, however, the blood level is probably an indication of the amount necessary to maintain an equilibrium with the required amounts in the tissues. If animals that have higher requirements also have higher tissue levels, it might be expected then that they would have higher blood levels. Sufficient data are available for thiamine, niacin, and folic acid to indicate that this is so (Figs. 1–3). A limited amount of data for the other B vitamins suggests similarly that smaller species have higher blood levels. Although considerable data are available for vitamins A, C, D, and E, they show little relationship to species size or to ecological factors. It would thus seem again that the B vitamins are distinguished from the other vitamins by the fact that smaller animal species tend to have higher blood levels. Moreover, the B vitamins and vitamin C in blood are most generally present in highest amounts in the cellular elements, whereas vitamins A, D, and E are predominantly in the plasma.

Tissue levels of vitamins in various species. It has been recognized for some time that the tissues of smaller animals tend to have higher B vitamin levels than the tissues of larger animals (*7*). Whereas the voluminous data available are adequate to insure the validity of this generalization, the concept is considerably hampered by the existence of numerous deviations from this trend, which are at present unexplainable. From a theoretical standpoint it seems entirely reasonable to expect that animals having a higher metabolic rate would require higher tissue levels of vitamins than animals having a lower metabolic rate. Moreover, if the logarithm of the oxygen consumption per gram of tissue is plotted against the thiamine (or other B vitamin) content of that tissue for even such diverse things as vertebrates, tissues of vertebrates, invertebrates, green plants, and bacteria, it is apparent that there is a definite correlation between the two factors. It is also apparent that when these factors are considered, the species fall into three major categories; the cold-blooded animals and green plants, which contain about 10 micrograms of thiamine per gram of wet tissue for every milliliter of oxygen consumed per gram of tissue per hour; the warm-blooded animals and their tissues, which contain about 1 microgram, and the aerobic bacteria, which contain from 0.1 to 0.001 microgram per gram of packed cells. Using even such rough conversion factors as these, it is possible to calculate the thiamine content of the diverse members of the first two groups from the oxygen consumption within about 50 percent of their actual values. The differences in these groups may be almost entirely attributed to the temperature effect in the cold-blooded animals and to the greater surface area of the bacteria.

This same tendency may be examined from another standpoint—that of the time taken for a species to reach maturity. Williams *et al.* (*8*) have shown that the protein level of milk varies among species in an inverse manner with the time required to reach maturity, and that the B vitamin levels in milk from various species vary in a similar manner. This relationship is of considerable interest in that it would seemingly be impossible were the trends previously considered not also true.

A final consideration in regard to tissue levels is the fact that in any given species, the B vitamin levels in specific organs and tissues follow closely the respiratory rates of these tissues. Exceptions occur in this case, which can generally be explained on the basis of specialized functions of the tissue or organ, but the B vitamin content is a fair indication of the over-all metabolic activity of the material in question.

The tissue and milk levels of vitamins A, C, D, E, and K vary among animal species largely in relation to dietary habit. Moreover, in the tissues of any given species, concentrations follow almost entirely the specialized functions and the storage abilities of the tissues. While data are somewhat limited in this regard, it is readily apparent that relationships depending upon species size and metabolic rates do not exist.

Conclusions. On the basis of nutritional requirements, distribution, and relationship to the metabolic rate, the vitamins fall into two distinct groups. One group includes those vitamins which have been classed as B vitamins, and which show themselves in a variety of ways to be intimately associated with the fundamental metabolic apparatus of living cells. A consideration of nutritional requirements, blood levels, tissue levels, and metabolic rates shows that these vitamins are associated in increased amounts with smaller species, whereas the remainder of the vitamins manifest no such relationships and appear to have only highly specialized functions for certain tissues and cell groups. A further comparative biochemical study of this group may do much to elucidate the specific functions of its members.

References

1. BENEDICT, F. G. *Carnegie Instn. Publ.*, 1938, **503**.
2. COWGILL, G. R. *The vitamin B requirement of man.* New Haven: Yale Univ. Press, 1934. P. 183.
3. ELVEHJEM, C. A. In Green, D. E., *Currents in biochemical research.* New York: Interscience, 1946. P. 79.
4. PETERSON, W. H. *Biol. Sympos.*, 1941, **5**, 31.
5. ROSENBERG, H. R. *The chemistry and physiology of the vitamins.* New York: Interscience, 1942. P. 96.
6. WILLIAMS, R. J. *J. biol. Chem.*, 1919, **38**, 465.
7. ———. *Vitamins and Hormones*, 1943, **1**, 229.
8. WILLIAMS, R. J., CHELDELIN, V. H., and MITCHELL, H. K. *Univ. Texas Publ. 4237*, 1942, 97.
9. WILLIAMS, R. J. *et al.* *The biochemistry of the B vitamins.* New York: Reinhold, in press.
10. WALD, G. *Harvey Lect.*, 1945–6, **41**, 117.
11. WOODS, A. M. *et al.* *Univ. Texas Publ. 4237*, 1942, 84.