Unique Characteristics and Implications of Individual Health Profiles*

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During the era of prescientific medicine, people were divided into two categories: those who were sick and those who were not sick. Physicians found it necessary to establish criteria to differentiate the ill and separate them according to symptoms and signs characteristic of classifiable diseases. Because of preoccupation with disease, the concept of the "normal" versus the pathological, as two opposite and definable conditions, was inevitable in the absence of scientific knowledge of human chemistry and physiology. This concept has carried over into the present era of scientific medicine. Growing health awareness and concern and the demand for preventive medicine, however, has sharply focused attention upon the question of normalcy. This vestigial desire for a neat, comfortable definition of "the normal" was initially satisfied by the artifact of utilizing the statistical mean and two standard deviations as descriptive of the "normal" population. As our knowledge of human physiology, chemistry and hematology has enlarged, however, critical analysis of precise measurements has demonstrated that there is no universal "normal" state, nor a "normal" range of values. *Normalcy* is a philosophical and social condition of not being recognized *abnormal.* Scientific definition of "normal" is not only impossible but meaningless. The large heart which is normal for a big man is decidedly abnormal for a small man. The normal erythrocyte count for a native of the high Andes is abnormal for a native of the Virginia tidelands. Furthermore, the body is seldom free of some reaction to bacterial invasion, foreign protein, or localized tissue destruction. Dr. Edmond A. Murphy (Perspect. Biol. Med., 15:566, 1972) asks what reason there is to believe that the notion of normalcy has any useful meaning. He questions the purpose of trying to convert a continuum of graded risk and change into a fictitious dichotomy of the normal and the abnormal.

There is a need, however, to recognize and describe the deterioration of optimum health in the individual person as a basis for rational preventive medicine and predictive diagnosis. The prerequisite is documentation of a reference base of values descriptive of optimum health of each individual.

The International Federation of Clinical Chemistry has established a committee on relative values to recommend definitions and procedures for determining reference values. This committee is agreed that the artificial concept of a normal average and normal range should be avoided and considered impossible to define scientifically. Preference is given the term "reference values," defined as those values of quantities which describe a definite "reference state" of health or disease of an individual or of a group of like people. The reference state may be that of optimum health defined by a given set of limits related to a person's genetic potential, environment and life habits, or of relatively good health, compromised only by stabilized defects which do not shorten survival. Other reference states related to disease are useful in diagnosis and monitoring therapy. Our present interest is focused on the reference state of optimum health.

Only in the past decade have laboratory meth-

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ods and automated instrumentation become precise enough to permit discovery of individual differences in homeostatic control of blood chemistry and physiology and of the consequent documentation of a reference profile of reliable values for each person. Work started at the National Institutes of Health during 1960, which is being continued in our Institute of Health Research,* has demonstrated that chronological profiles of blood chemical, hematological, and certain physiological measurements are unique for each individual and are surprisingly stable over prolonged periods. Such a profile, when established during a time of vigorous health and well-being, becomes a clearly defined and reliable reference base for all future measurements, and more importantly, for the discovery of early abnormal trends in that particular person. We have found that the individual range of variation for each constituent, when corrected for laboratory bias, is quite small, stable and far less than the range of values found to be usual in a large population of "well" people.

Documentation of Individual Reference Profiles. Because test methods are not sufficiently precise, it is necessary to obtain a series of repeated sets of measurements during a period of optimum health for any given person, in order to establish his individual reference values of blood chemistry, hematology and physiology. The series of measurement data permits the determination of the mean and the range of variation of each measurement to best approach the true values. Since it has been clearly demonstrated in our laboratories, and confirmed by others, that the observed range of repeated measurements of blood chemical constituents consists of at least two components, the bias of laboratory manipulations and a physiological variation, all sets of observed measurements should be corrected for the analytical bias. Physiological shifts are characteristic of the person being tested. Laboratory manipulations, instruments and conditions cause analytical bias. For most blood chemical tests, this bias is at least as large as, and for some tests substantially larger than, the physiological variation manifested over periods of weeks or months. This is illustrated in figure 1, which is the plot of cholesterol values obtained weekly for 12 weeks on a group of 29 healthy individuals. The horizontal axis represents the range of two standard deviations, above and below the mean, for the entire group of 200 healthy persons in the study. Each bar represents the mean and standard deviation of the observed set of values for that individual. The middle, darker portion represents the physiological changes which occurred over the period of observation and the open ends are the proportion of the total variation due to analytical bias. This plot also illustrates the uniqueness of the mean and physiological variation for each individual.

We have interpreted the range of variation in each person to portray a long-term homeostatic control of the particular blood constituent. This shows the individual's healthy tolerance limits and built-in control of variation, based on his genetic potential and the usual circumstances for his life-style in terms of diet, physical activity and reaction to his environment.

The variation of any blood constituent in an individual apparently is controlled by physiological feedback communication mechanisms limiting the degree of variation. The range of values established during a period of optimum health may be presumed to represent the efficiency of this control and is assumed to be homeostatic in nature. Homeostatic control apparently is effective in the individual over long periods of time (years) for many blood con-

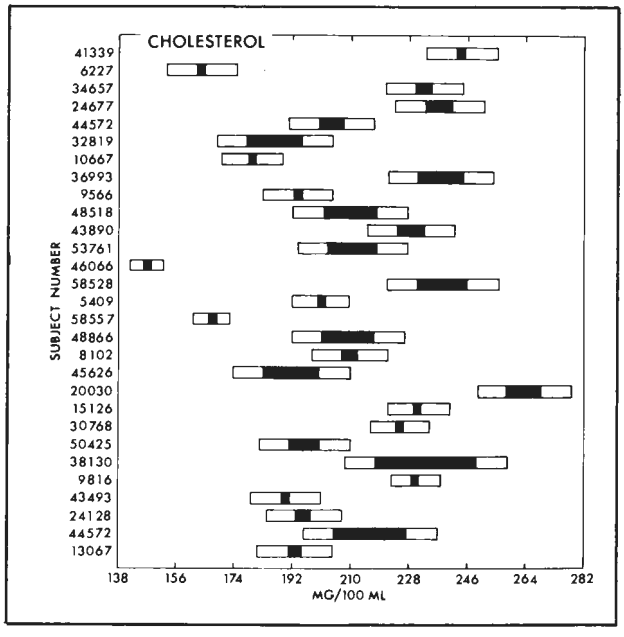

Fig. 1—Blood cholesterol values of 29 healthy people. Each bar represents the mean and 2.5 standard deviation ranges of the 12 weekly measurements for each person. The open portion at both ends of each bar represents the measured laboratory bias of the test.

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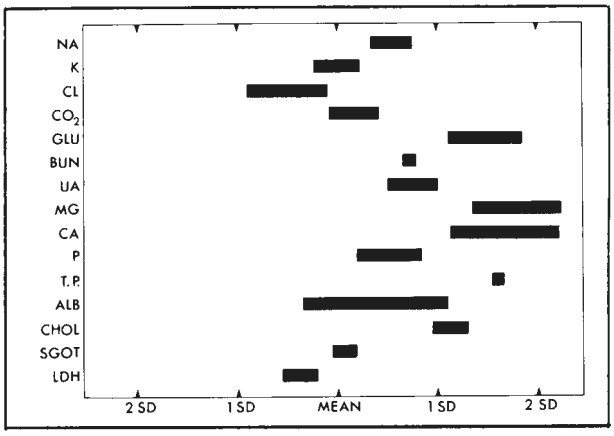

Fig. 2

stituents. It is reasonable to believe that the degree of this homeostatic control of the range of variation must have important implications in relation to state of health and optimum function. Thus, substantial changes in the range of variation of a blood chemical must have medical meaning; for instance, for a consistently narrow range of glucose or uric acid or cholesterol or an enzyme to broaden to a wide range of daily or weekly variation may augur trouble.

When repeated measurements obtained are similar for other blood chemical constituents over a defined period of optimum health, and the data are plotted in a like manner, the resulting chart depicts the unique blood chemical profile for that individual. Figures 2 and 3 are the profiles of two people. No two identical profiles have been found in several hundred healthy people.

Such a set of quantitative values, when established with rigidly controlled, precise analytical methods during a period of optimum health, constitutes the individual's reference base line to which all subsequent values can be compared. Deviation of any particular constituent or set outside the individual's reference range may be presumed to be undesirable for this particular person—even though the deviation may not extend beyond the conventionally accepted boundaries of "normal" for the general population. Should several determinations, at appropriate intervals, confirm the deviation to remain outside this individual's reference range, it should be interpreted as the beginning of a definite pathologic trend, although otherwise undetectable, that requires further investigation.

The "natural history" of the deterioration of an optimum state of health associated with the development and onset of disease may be depicted diagrammatically as in figure 4. During some period of a person's life, prior to onset of symptoms, there are at least two phases—optimum health and a zone of uncertainty during which health gradually and "silently" deteriorates to a condition of "predisease." This phase may be detectable by predisease changes in chemical and physiological quantitative values by comparison with the person's health reference profile of values and variations.

Figure 5 represents two possible deviation events. Superimposed upon the healthy reference profile of an individual are the results of annual sets

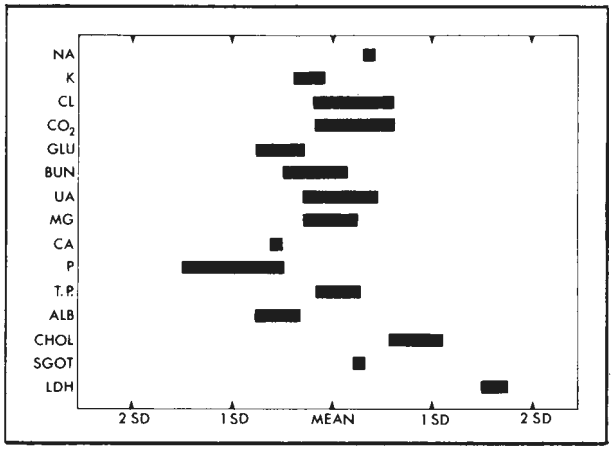

Fig. 3

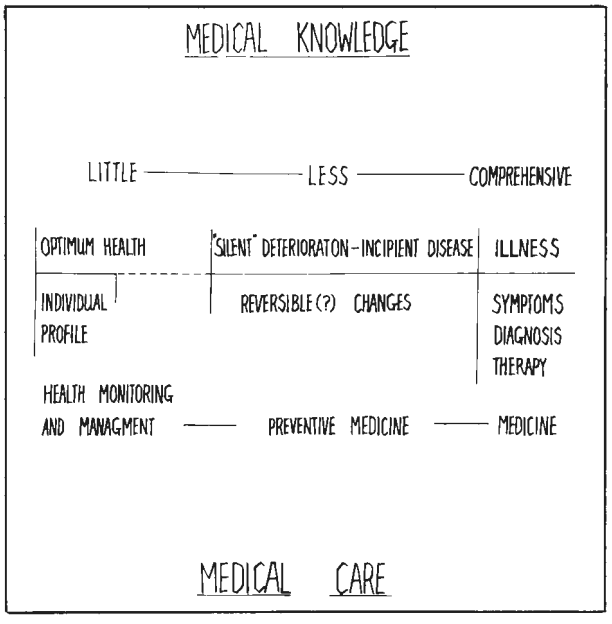

Fig. 4

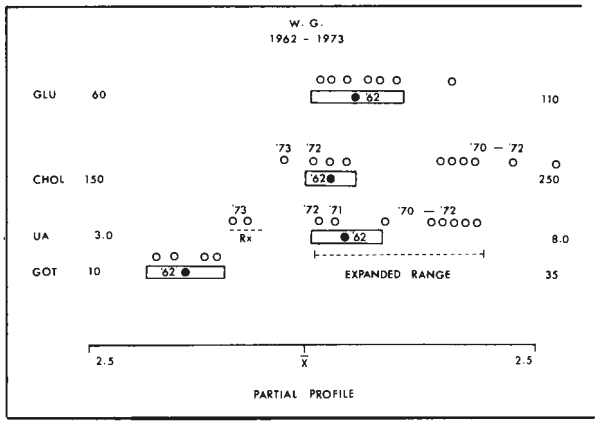

Fig. 5

of tests for several years. Note that in the instance of uric acid there is a linear and persistent deviation of these results in the direction of higher values. For cholesterol, deviation is geometric in progression. Even though these results are all within the range usually considered normal for an adult, in this instance, they must be interpreted as definitely abnormal for this particular person. Here we have a new tool for monitoring a person's health and for detecting early trends in the deterioration of his health, which may warn of impending pathology. Furthermore, this technique allows rationalized management procedures to attempt reversal of early abnormal trends or correction of the conditions which brought about this change. Figure 6 is the chronological graphic record of such a case over a ten-year period. There was a gradual increase in blood uric acid and cholesterol for several years, followed by reversal of both to the individual's own normal range

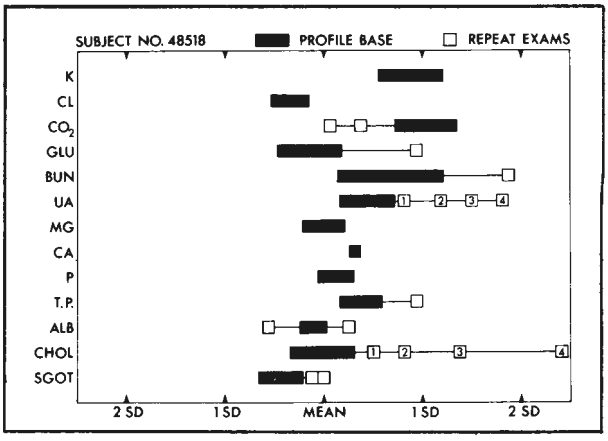

Fig. 6

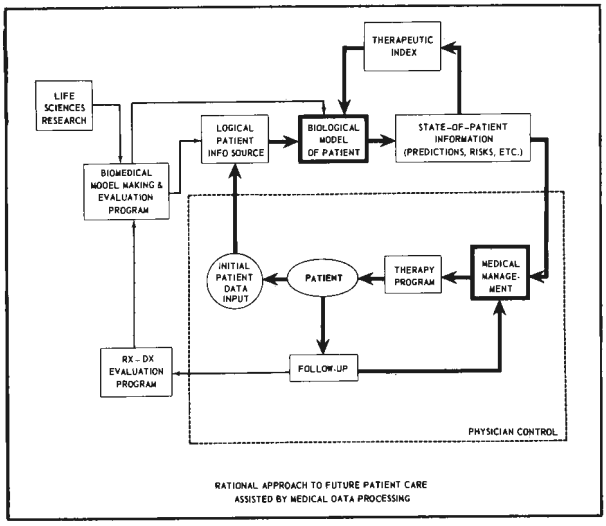

Fig. 7

by institution of management procedures, including monitored administration of allopurinol and a diet and running exercise regimen. Other cases in our experience encourage the belief that such "silent" trends can be discovered during a reversible phase and may result in either delay or prevention of progressive deterioration to overt disease.

The Future. We now have a scientific procedure for establishing a reference base of optimal values for people and the maintenance of prospective, lifetime profiles in regional data centers. It is possible to design computer simulation models for each of these profiles, including the body chemistry, physiology, and later, mental and emotional test patterns to be correlated with the person's life history. The individual models can be updated periodically to provide follow-up health management guides for each person. Such a data base will be invaluable for the physician in guiding his diagnostic and therapeutic decisions when a person requires medical care. Figure 7 is a tentative diagram of such a model. When irreversible changes do occur and definitive diagnosis is feasible, the development of disease will be detected far earlier than is now possible and presumably the patient will react more amenably to rational therapy. The physician team will have at hand not only a subjective, recent history but also a well-documented family and clinical history and a very useful physiological and chemical history. This is only one of the many advances we may expect of rapidly accelerating technological progress in the new era of preventive medicine.

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