Matsuya, S. Bloom, A. Robbins, H. Green, *Wistar Inst. Symp. Monogr.* No. 7, 87 (1967).
12. E. B. Smith and R. S. Slater, *Lancet* **1972-I**, 463 (1972).
13. R. Ross and J. A. Glomset, unpublished data.
14. R. Ross, T. Wight, J. Glomset, M. Riddle, unpublished data.
15. R. Ross and S. J. Klebanoff, *J. Cell Biol.* **50**, 159 (1971); J. Kunz, D. Kranz, O. Keim, *Virchows Arch. Abt. A, Pathol. Anat.* **342**, 345 (1967); R. C. Buck, in *Atherosclerosis and Its Origin*, M. Sandler and G. H. Bourne, Eds. (Academic Press, New York, 1963); R. W. Wissler, *Circulation* **36**, 1 (1967).
16. R. Ross, in *Treatise on Collagen*, B. S. Gould, Ed. (Academic Press, New York, 1968), vol. 2, pp. 1–82.
17. E. R. Dalferes, Jr., and H. Ruiz, *Atherosclerosis* **13**, 121 (1971); S. A. Bencosme and J. U. Nalis, *Exp. Mol. Pathol.* **6**, 300 (1967).
18. F. Parker and G. F. Odland, *Amer. J. Pathol.* **48**, 451 (1966).
19. D. Layman and S. Narayanan, unpublished data.
20. T. Wight, unpublished data.
21. W. B. Kannel, M. J. Garcia, P. M. McNamara, G. Pearson, *Human Pathol.* **2**, 129 (1971).
22. S. R. Srinivasan, S. A. Lopez, B. Radakrishnamurthy, G. S. Berenson, *Atherosclerosis* **12**, 321 (1970); P.-H. Iverius, *J. Biol. Chem.* **247**, 2607 (1972).
23. D. M. Kramsch, G. Franzblau, W. Hollander, *J. Clin. Invest.* **50**, 1666, 1677 (1971).
24. L. E. Duncan, in *Evolution of the Atherosclerotic Plaque*, R. J. Jones, Ed. (Univ. of Chicago Press, Chicago, 1963).
25. M. D. Haust, in *Atherosclerosis: Proceedings of the Second International Symposium*, R. J. Jones, Ed. (Springer-Verlag, New York, 1970), pp. 12–20.
26. R. Virchow, in *Gesammelte Abhandhungen zur Wissenschaftlichen Medicin* (Meidinger Sohn, Frankfurt-am-Main, 1856), p. 458.
27. N. N. Anitschkow, *Beitr. Path. Anat. Allg. Pathol.* **56**, 379 (1913).
28. ——— and S. Chalatov, *Zentralbl. Allg. Pathol.* **24**, 1 (1913).
29. O. W. Portman and M. Alexander, *J. Lipid Res.* **11**, 23 (1970); R. L. Robinson, K. C. Hayes, H. L. McComb, T. P. Faherty, *Exp. Mol. Pathol.* **15**, 281 (1971); P. J. Manning and T. B. Clarkson, *ibid.* **17**, 38 (1972).
30. E. B. Smith, *J. Atheroscl. Res.* **5**, 224 (1965).
31. S. Dayton and S. Hashimoto, *Exp. Mol. Pathol.* **13**, 253 (1970); P. J. Scott and P. J. Hurley, *Atherosclerosis* **11**, 77 (1970).
32. This study was supported by grants HL 14823, RR 00166, and HD 04872 from the National Institutes of Health. We thank Dr. Frank Parker for his help and Dr. Michael Stemerman with whom the initial studies in vivo were performed. We are indebted to Beverly Kariya, Lynne Phillips, Mary Stewart, and Eunice Wong for their technical assistance.

Health Care Delivery and Advanced Technology

A more significant role is proposed for those who develop technology.

Charles D. Scott

The current drive to upgrade the health care delivery system lacks a vital factor—significant involvement of those who develop new technology. A whole spectrum of development engineers and applied scientists is necessary to provide support for any massive venture requiring the development and application of advanced technology, and this is exactly the kind of effort that will be necessary to help solve our "health care crisis." Further, the effective implementation of such an involvement will require the integration of many elements in biomedical science and engineering into well-defined, multidisciplinary teams organized to solve specific problems.

The problems associated with the delivery of health care have sometimes been compared with the problem that the National Aeronautics and Space Administration (NASA) faced in sending men to the moon, or with the concentrated, cooperative effort necessary for developing a viable nuclear energy industry. These are examples of Herculean endeavors that required the development of advanced technology to successfully achieve national goals. In each of these examples, the objective was realized when engineers and applied scientists became intimately involved with the problems, not only on an operational basis, but also in the formative and conceptual phases.

Development personnel are not effectively employed when the problems are narrowly defined and when the allowable solutions lie only within the realm that is well known to the more basic scientist or scientific administrator. In the biomedical area, all too often a contract approach has been used, where the engineer is contracted to add the details to a preconceived technological concept. As a result, the innovative development engineer has not been attracted to this area, and much of the resulting technology has not been founded on the best engineering principles.

It is true that we have spent, and are still spending, vast sums of money in the general area of health care. Large amounts are allotted by the National Institutes of Health (NIH) for studying the causes of disease; billions are disbursed every year for medical services; and the number and sophistication of our current health care facilities are being increased by the Health Services and Mental Health Administration (HSMHA). However, the amount spent on research and development for health care delivery by the federal government through the Department of Health, Education, and Welfare (HEW), recently estimated to be \$18 to \$59 million per year (*1*), is very small in comparison. The higher figure also includes funds used for the development of manpower, system analyses of alternative plans, and so forth. This by no means represents a national commitment or dedication to solving the health care problem, at least in the same sense that we committed ourselves to traveling to the moon or developing nuclear energy.

An additional point should be stressed. We will not achieve an "ultimate" health care delivery system, although we must maintain a continuing effort in this direction. For as new insights into the prevention and treatment of diseases are attained through biomedical research, they must also be applied to the health care of the general population.

Why "Advanced" Technology?

The patient frequently points to two major problems in his involvement with the health care delivery system: the unresponsiveness of the system and the high cost. The first problem manifests itself in the difficulty of entering the health care system,

The author is chief of the Biochemical Technology Section, Oak Ridge National Laboratory (operated by Union Carbide Corporation for the U.S. Atomic Energy Commission), Oak Ridge, Tennessee 37830, and part-time professor of biomedical engineering, University of Tennessee, Knoxville.

particularly in a remote area (one in which the population density is too low to allow optimum operation of a major medical center), but it is also demonstrated within the system, where one finds, in some cases, that the orientation is toward optimizing the use of facilities instead of optimizing the service to the patient. Considering the second point, costs of treating the critically ill will undoubtedly continue to increase; therefore, the only hope for decreasing health care costs is, apparently, to decrease the necessity of hospitalization. Obviously research and development in health care must include consideration of these problems.

A major thesis has seemed to be that sufficient biomedical technology is now available for health care delivery and that, therefore, efforts should be directed toward efficiently applying existing technology in a well-managed environment. According to this reasoning, emphasis should be centered on securing more efficient organization and management of health care facilities or on reproducing existing facilities. Thereafter, more effective usage of the facilities and the data they generate should be implemented by increased application of computer techniques and better management. Although these may seem to be obvious and desirable approaches, they alone are not adequate to solve all problems of health care delivery, and they certainly cannot, independently, ensure the application of advances in biomedical research to the general health care system.

Many technological innovations have been introduced in the biomedical area in recent years, particularly with regard to the development of new surgical tools and materials, electronic monitoring devices, and other devices for diagnosis and treatment of the critically ill. However, much of the technology applied to health care delivery systems has been "catch up" in nature; that is, technology originally developed for other scientific areas has been adapted to the health care system, frequently as an adjunct to automating manual tasks. As a result, large sums of money have been spent in automating or mechanizing portions of clinical laboratories, and computers are becoming commonplace in most large hospitals in an attempt to solve the data processing problems. These have been important developments, and they are largely responsible for the higher quality of patient care, at least in large medical centers; however, they have not begun to correct all of the deficiencies in health care delivery.

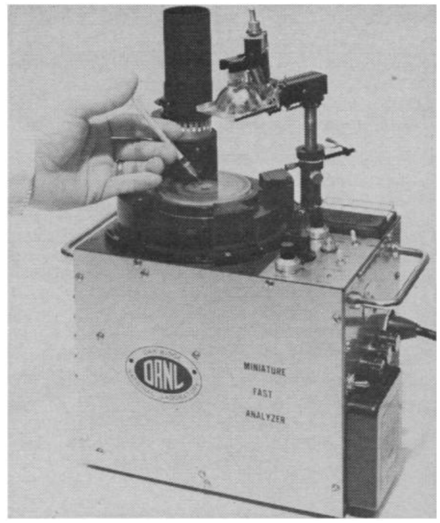

Fig. 1. Introduction of a whole blood sample into a miniature fast analyzer for the automated analyses of several chemical constituents (*2*, p. 751; *3*, p. 754).

Obviously, we must continue to adapt and use any technology that will help meet our goals, regardless of its derivation. Thus, "spin-off" from advanced technology generated in unrelated programs should always be encouraged, even though the possibility of spin-off is not a sufficient reason for continuing those programs. The next phase in obtaining better health care delivery will require the solution of problems unique to the health care system, and this will, in turn, require technology that can be specifically addressed to those problems. The technology developed for these problem areas should be of sufficiently high caliber to have a significant spin-off value of its own. Such developments would indeed represent "advanced technology."

As examples, it is interesting to consider two areas that have not been seriously approached, mainly because they will necessitate entirely new technological concepts, along with additional financial support. These are (i) the delivery of high-quality health care in special situations, including emergency services, outpatient care, and health care delivery to areas remote from large medical centers, and (ii) preventive medical care.

Special Health Care Areas

Most of the recent technological developments in health care delivery have been oriented toward increasing the efficiency of operation of the major medical center for critically ill individuals. For example, centralization, mechanization, and computerization of clinical laboratories have resulted in relatively low costs for analytical results; on the other hand, low costs have not necessarily led to effective use of these results, especially in the many special situations existing in the health care system. Little attention has been given to the problem of providing rapid and high-quality analytical services for emergency situations and for the critically ill. In these cases, the advantage of an efficiently operating central laboratory with automated data processing is lost if acquisition of the results requires several hours. Similarly, the outpatient spends a considerable amount of his time simply waiting for the results on which his diagnosis and treatment will depend. Finally, the efficient operation of a large, expertly staffed medical center has practically no bearing on the delivery of health care to remote areas. In such situations, automated analytical systems that can operate economically are still important but, so far, unavailable.

An example of a recent technological development that may be useful in these areas is the small, automated fast analyzer, which will be capable of providing rapid analyses of many constituents in blood (*2*, *3*). In such a system, a sample of whole blood may be injected directly into the analyzer without preparation, and analytical results for several biochemical indicators of abnormality can be obtained (Fig. 1). A system of this type could be used in emergency treatment (even at the bedside), in remote areas, in small clinics, or in outpatient facilities, since it will be portable and can provide precise results within a few minutes after the blood sample is injected. This development, supported by the National Institute of General Medical Sciences (NIGMS), NASA, and the Atomic Energy Commission, represents a very small portion of the development effort that could be effective in special health care areas.

Preventive Health Care

Preventive health care may result in an ultimate decrease in the cost of health care services, for it is possible that expensive hospitalization can be avoided by detection and treatment of incipient disease. Although biomedical research is beginning to develop insights that may allow this approach, technology has not been developed to effectively expedite preventive health care. Programs that provide multiphasic screening of a select population have demonstrated that multiple laboratory tests can uncover unsuspected health problems (*4*). Unfortunately, such screening programs, when applied to the "healthy" population, face a severe limitation: in general, the technology used is exactly the same as that developed for treating the critically ill, and therefore the diagnostic aids are not always sufficiently sensitive to detect incipient disease. Although multiphasic screening can be discredited as nonproductive or at least uneconomic (*5*), it is not an incorrect health care concept—rather, the lack of proper technology prevents effective implementation.

It is now generally accepted that the majority of human diseases will ultimately be understood and controlled at the molecular level. Evidence indicates that hundreds of the molecular constituents of physiological materials may have pathological importance. For example, in a recent annotated bibliography on urinary constituents of low molecular weight, the literature of a 3-year period contained more than 3000 citations to over 700 urinary constituents that were thought to be important (*6*). Many of these are known to be biochemical indicators of abnormality and, in some cases, multiple indicators will allow a further differentiation of the specific disease, even in early stages. If the various body fluids could be economically monitored for their biochemical spectrum, this information could be used to screen subjects for literally hundreds of abnormalities. Further, if the systems were sensitive enough, they could determine abnormalities at a very early stage.

High-resolution chromatographic systems are being developed to provide such analytical data. These include both gas chromatographic systems (*7*) and new, automated liquid chromatographs (*8*). Examples of the latter are high-pressure ion-exchange chromatographs that can be used to automatically determine hundreds of the molecular constituents of body fluids (*8, 9*). Development of these systems was supported by the NIGMS and they are now being evaluated in several laboratories. A recent innovation is the use of differential chromatography for automatically comparing the constituents of the body fluids of one subject with those of other, clinically normal subjects to determine the differences and their significance (*10*) (Fig. 2). The effects

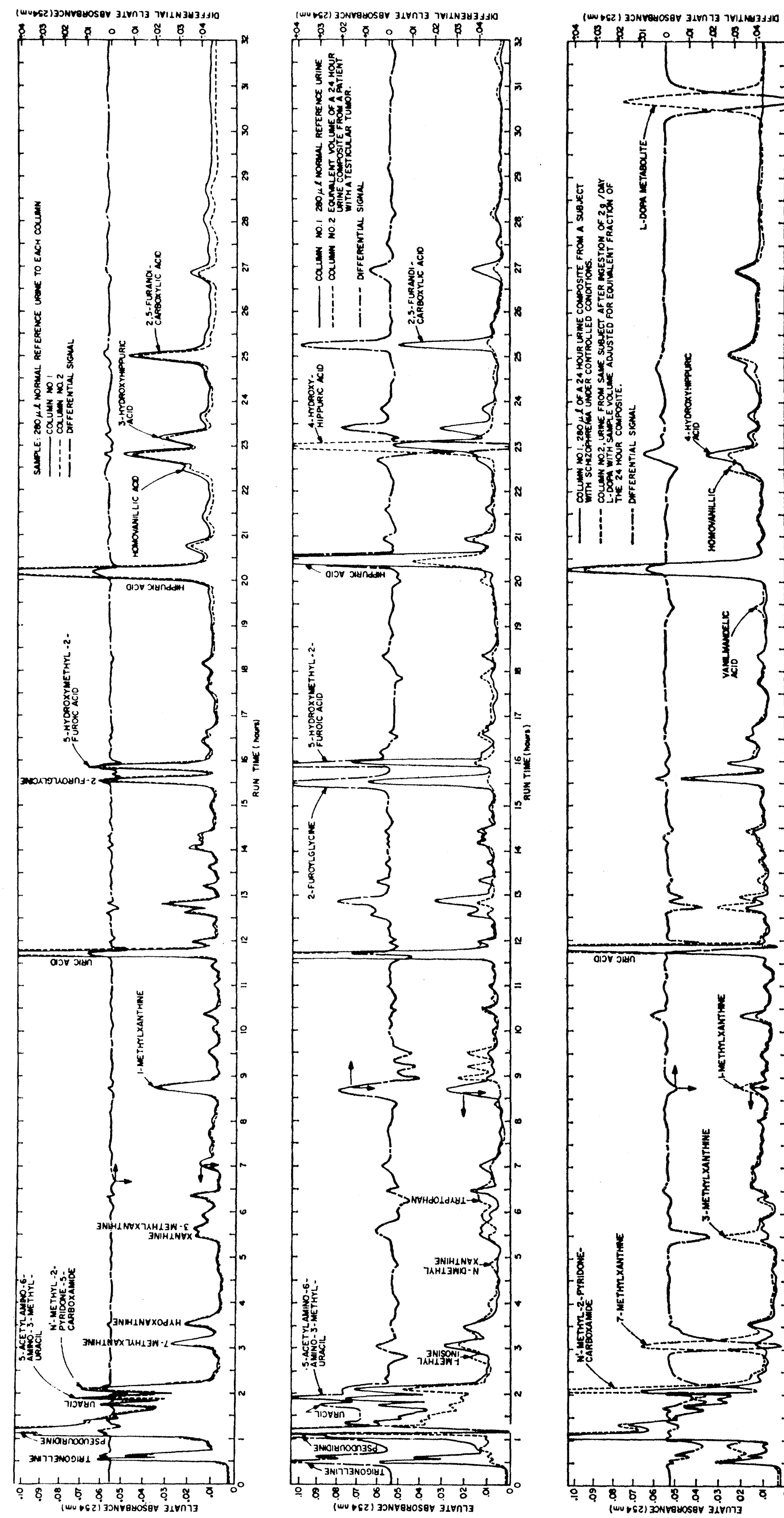

Fig. 2. Automated, high-resolution differential chromatography of the ultraviolet-absorbing molecular constituents of body fluids, showing differences between urine samples from normal subjects and those with pathologies and the influence of therapy on the urinary biochemical spectrum (*10*, p. 743). [Oak Ridge National Laboratory drawing 72-3221R4]

of therapy can be biochemically monitored by differential analyses of samples taken before and after treatment. This type of technology is still in its infancy and is not ready for widespread use; however, this is another area of advanced technology that could be effectively exploited. The point is that the development of technological advances is not limited by lack of concepts and personnel, but by the lack of the commitment of our present resources to that task.

Manpower Requirements

It has been suggested that many more physicians, as well as various paramedical personnel, are needed to ensure adequate health care delivery. Indeed, our educational institutions have been making preparations to meet these needs. Conversely, our present pool of engineers and applied scientists appears to be sufficiently large to provide high-quality workers for future technological needs in the delivery of health care without extensive additional manpower. Of course, it will be necessary to have some people who are trained in both technology and the biomedical sciences to help bridge the gap that will be created when engineers invade a new area. Several universities now have educational programs for biomedical engineers, and a relatively large number of engineers and applied scientists who have been involved in the biomedical areas during the last few years could effectively serve in this capacity also. Primarily, though, the same types of engineers used in other areas can be effectively used in the health care effort, and at the present time there seems to be an oversupply of such talent. Electrical and instrument engineers can develop new instrumentation requiring advanced electronics; chemical engineers and development chemists can contribute knowledge concerning biochemical separations and chemical assay methods; computer specialists can apply computer technology to health care problems; and so on. Again, all that is lacking is the decision to proceed.

It has been pointed out that physicians and other biomedical scientists are not always sympathetic to the technological approach for solving biomedical problems (*11*). This is undoubtedly true. Similar situations existed in the past when those developing technology became involved in an area previously considered the domain of the scientist. For example, many problems developed when theoretical physicists and engineers first began working together in the field of atomic energy (*12*), but progress in that field would not have been made without the massive technological developments that resulted. The necessary interaction between these two groups had, in some cases, to be forcefully encouraged. Likewise, the engineer, the physician, and the biomedical scientist must work together to solve important problems that affect the entire population.

Organization

The health care system has diffuse boundaries, cutting across a wide sector of the scientific-technical community, both private and governmental. As Schwartz recently indicated (*13*), it will be extremely difficult to provide the analysis of the health care system that will be necessary for properly arriving at new policy. Organizing resources to achieve good health care will also be difficult, but it is obvious that the present effort in this area could be expanded.

Some principles for organizing the technological effort for health care delivery can be outlined, based on previous, successful technological endeavors: (i) development personnel must be well integrated into the health care system, since most of the problems that are apparent will require a multidisciplinary solution and all components of the development team must be involved in the definition of the problems as well as in the associated technical management; (ii) the federal bureaucracy monitoring the program must be sympathetic toward maintaining a cohesive effort, with limited segmentation, and an effort must be made to ensure continuity of the development effort; (iii) a significant portion of the development effort, whether intramural or extramural to the monitoring federal agency, must be in an institution or institutions whose primary functions are the development of technology and the solution of problems; (iv) management associated with the development of advanced technology must be required to have extensive contacts with other aspects of the health care system and with all areas of biomedical research; and (v) the mission of the overall management must not be so diffuse that technological development is easily canceled or ignored in preference to other areas.

The most logical governmental department for this organization is HEW, since there is already a significant involvement of several segments of that agency. Very useful technological advances have been made within the NIH, and some funds are available in HSMHA for this purpose. Either of these institutions could be given additional funds for the purpose of assuming this development function, or an entirely new organization within HEW could be created. In either case, development would be successful only if the additional technological efforts are given at least equal priority with existing programs in the health care delivery field.

Summary

Remedying the deficiencies in the current health care delivery system and effectively using advances in biomedical research require that a significant effort be organized to develop advanced technology in this field. The time is ripe and development personnel are available; hence, what are needed are simply a dedication to solving the problem, a commitment of resources toward this end, and an organizational mode that will allow the effective participation of developmental personnel.

References

1. W. Bevan, *Science* **173**, 985 (1971); M. K. DuVal, *ibid*. **175**, 1311 (1972).
2. C. D. Scott and J. C. Mailen, *Clin. Chem.* **18**, 749 (1972).
3. C. A. Burtis, J. C. Mailen, W. F. Johnson, C. D. Scott, T. O. Tiffany, *ibid*., p. 753.
4. D. M. Young and N. Drake, in *Automation in Analytical Chemistry, Technicon Symposia 1965*, L. T. Skeggs, Ed. (Mediad, New York, 1966), p. 427; D. J. Bryan, J. L. Werne, A. Vian, A. W. Musser, F. W. Schoonmaker, R. E. Thiers, *Clin. Chem.* **12**, 137 (1966).
5. W. P. Fleeson and R. E. Wenk, *Postgrad. Med.* **48**, 59 (1970).
6. S. Katz *et al*., *Annotated Bibliography of Low-Molecular-Weight Constituents of Human Urine* (AEC report ORNL-TM-2394, Oak Ridge National Laboratory, Oak Ridge, Tenn., 1968).
7. H. W. Street, *Advan. Clin. Chem.* **12**, 217 (1969); E. Jellum, O. Stokke, L. Eldjarn, *Clin. Chem.* **18**, 800 (1972).
8. W. W. Pitt, C. D. Scott, W. F. Johnson, G. Jones, *ibid*. **16**, 657 (1970).
9. S. Katz, S. R. Dinsmore, W. W. Pitt, *ibid*. **17**, 701 (1971); C. D. Scott, *Advan. Clin. Chem.* **15**, 1 (1972).
10. C. D. Scott and W. W. Pitt, *J. Chromatogr. Sci.* **10**, 740 (1972).
11. R. F. Rushmer and L. L. Huntsman, *Science* **167**, 840 (1970).
12. S. Groueff, *Manhattan Project—The Untold Story of the Making of the Atomic Bomb* (Little, Brown, Boston, 1967).
13. W. B. Schwartz, *Science* **177**, 967 (1972).