course, only one of the problems facing eastern Kentucky and areas like it in the Appalachians. Coal mining and its subsidiary activities have dominated the economy. The rough terrain is an isolating factor, and the power and communications systems in the area are poorly developed.

Development of the Appalachian area, however, is now getting more serious attention than it ever has before.

John F. Kennedy seems to have been lastingly disturbed by what he saw, in 1960 as he campaigned in the hills of West Virginia, a state which gave him a crucial primary victory.

In Congress, Representative Carl D. Perkins (D-Ky.), whose district includes the northeastern tier of the coal counties of the plateau, has been working with what he feels is increasing effectiveness for a major resource and economic development program for the Appalachian Highlands area.

Perkins's bill provides for the formation of an Appalachian Highlands Commission composed of federal agencies and representatives appointed by the governors of the 11 states in the region. This commission would formulate plans for the development of the area, and Perkins hopes that an interstate compact would be eventually formed by the Appalachian states to facilitate development. The development plan would include improved flood-prevention and flood-control measures and a whole range of industrial and community development, conservation, and public health programs.

Assessing the Problem

In April, a President's Appalachian Regional Commission (PARC) was set up, with Franklin D. Roosevelt, Jr., Under Secretary of Commerce, as chairman. The Conference of Appalachian Governors and the federal government's Area Redevelopment Agency apparently urged that a special regional development program is required if the region is to offer adequate opportunities to its inhabitants and is to contribute more to the national economy.

A number of team surveys on different subjects—transportation, water resources, human resources, and so on—are under way now, and reports are scheduled to be submitted, along with recommendations for action, to the President by 1 January. Formulation of a comprehensive development program is to follow.

Besides Kentucky, the states now included in PARC are Alabama, Georgia, Maryland, North Carolina, Pennsylvania, Tennessee, Virginia, and West Virginia.

Caudill, in his book, calls for a regional development effort modeled on the Tennessee Valley Authority, though the precedent of T.V.A. may not be directly applicable, since the "miracle of T.V.A." was based on the production of low-cost hydroelectric power and there seem to be few major undeveloped waterpower sites in the region.

When Caudill calls for a major resettlement of the mountaineers he broaches a highly sensitive political subject. He argues that the population is too large and thinly spread, and that "metropolitanization" would make it possible to give people better housing, education, and opportunities for jobs. He adds that surplus workers should be trained and relocated in more prosperous areas. However reasonable the idea, such action by government is not popular with the voters, and relocation has been regarded as a fatal word politically.

Caudill's book has been criticized on and off the record, by those who know the region and its history, for exaggerations and oversimplifications. Scholars of the Western migration and settlement apparently may take exception to some of his generalizations. And Eastern Kentuckians may resent his picture of their past and present. Caudill has some prior experience as a critic not greatly honored in his own country and is unlikely to be deterred.

But the area planners can read Caudill's book with profit. By portraying the troubles of today as the harvest of history, he suggests the depth of the problems afflicting the region.

Federal participation in the redevelopment program, no matter how massive, must be done in full cooperation with state and local and private agencies. And to do what seems necessary to transform the Appalachians would appear to require an almost miraculous change of heart among many state legislators, county officials, and influential private citizens.

For Caudill may have struck the heart of the problem near the end of his book when he discusses, without brimming optimism, the task facing a Southern Mountain Authority. "To modernize the plateau," says Caudill, "the authority would have to tackle the complex tasks of modernizing the units of government which control its public affairs."—JOHN WALSH

Enovid: Contraceptive Pill and Recent FDA Report Clearing It Stir Continued Medical Dispute

The hope of the Food and Drug Administration that, by seeking the advice of a panel of medical experts, it could settle the controversy surrounding the oral contraceptive Enovid is not about to be fulfilled. On the contrary, the report of the special committee, headed by Irving S. Wright of Cornell Medical College, and FDA's decision, based on the report, to sanction continued prescription sale of the pill, have left as much medical uneasiness as they have quieted.

At issue is a question that has been raised about Enovid since it came into use as a contraceptive in the summer of 1960—namely, whether there is a relationship between use of the drug and thromboembolic conditions (blood clots). The Wright committee found insufficient statistical data to permit an evaluation of the overall relation between Enovid and thromboembolism, but it was able to analyze the relation between use of Enovid and deaths resulting from thromboembolic conditions. The committee, though it stressed the paucity of statistics and asked that its results be accepted with caution, found that death rates from thromboembolism appeared to be significantly higher for users than for nonusers of Enovid above the age of 35 (*Science*, 16 August, p. 621).

After receiving the report, the FDA extended from 2 to 4 years the period for which use of Enovid is recommended, and it also requested G. D. Searle, the manufacturer, to make certain changes in its medical literature regarding the drug. In the same statement, issued on 4 August, the FDA announced that available data on the long-term effects of Enovid left something to be desired, and it suggested that further studies with the drug be begun.

A possible discrepancy between the Wright report and the agency's action was noted in this space on 16 August. Since then, the report itself has come under criticism, principally from a few independent practicing physicians who found that it did not tally with their own experiences with Enovid. The critics are not a united band, but separate individuals who find themselves on common ground with regard to the Wright report: they disagree with its methods, question the com-

prehensiveness of its data, and think the committee too casual in its estimation of the safety of a drug currently being used by between 1½ and 2 million women. These doctors have been trying to call the FDA's attention to three points.

1) *Statistical method.* The Wright committee weighed 12 deaths from thromboembolism among 1 million "women-users" of Enovid during 1962 against the yearly incidence of fatal thromboembolism among comparable nonusers. They found a 12.1 incidence of fatalities among users, an 8.4 incidence among the general population. This difference was not regarded as significant on an overall basis, but breakdown into age groups revealed an increased risk for women over 35. No attempt was made in this analysis to distinguish a woman who had taken Enovid for 20 days from one who had taken it for 200. A woman who had taken Enovid for only 1 month was thus assumed to incur the same risk of thromboembolism as a woman who had not used Enovid over a 12-month period.

Method in Dispute

A more relevant statistical method, according to the report's critics, is the "woman-year" method, in which a woman-year of Enovid users (12 women taking the drug for 1 month each) is weighed against a woman-year of nonusers. This method takes account of an apparently high drop-out rate among Enovid users. The woman-year concept was employed by a conference of experts called by Searle in September 1962 to evaluate early reports of thromboembolism among patients taking Enovid; it is a method accepted by the FDA; and it is a method commonly referred to in Searle's advertisements for its product. Although there have been several attempts to discover why the woman-year concept was abandoned in the Wright committee's analysis, so far there has been no explanation. The FDA refers inquiries to Wright; Wright replies that the report was the work of competent statisticians who knew what they were about.

Edmond Kassouf, a New Jersey physician who has been a particularly vigorous critic of the report, has prepared a refutation of it with the help of a cousin-mathematician, Sheen Kassouf, of New York. According to Dr. Kassouf, if the woman-year concept had been used by the Wright committee, the death rate from thromboembolism among Enovid users would have been 22.3 per million per year, nearly three times as high as in the general population and of statistical significance for all age groups. Kassouf points out that the woman-year concept is still used by Searle, and he has asked the question, "can both the woman-user and woman-year concepts be right?"

2) *Puerto Rican deaths.* The Wright committee, its critics point out, as well as the 1962 Searle conference on Enovid, excluded from consideration three sudden deaths known to have occurred among a relatively small group of users of Enovid in Puerto Rico. Full medical reports on the deaths in Puerto Rico, where Searle's early clinical trials were carried out, were unavailable.

Although it is true that this information was excluded, and its absence may add weight to skepticism about Enovid, the blame should properly be lodged against the company's methods of record keeping during the investigational period, and not against the committee, which had to make the best of whatever data it could assemble. The committee had difficulties enough in gathering figures on mortality from thromboembolism for the continental United States, and in fact had data covering only 60 percent of such deaths. For Puerto Rico it was impossible to obtain similar information to use as a control, and even the three deaths in question were not certified as having resulted from thromboembolism. In the absence of reliable data, the committee, according to Wright, felt it had no choice but to leave Puerto Rico out of account.

3) *What is a valid comparison?* Finally, critics of the Wright report dispute its suggestion, echoed by the FDA and by several physicians interviewed by a New York medical paper, *Medical Tribune*, distributed free to doctors, that the risks of Enovid should be weighed against the risks of pregnancy and abortion. Although Enovid is uniquely effective and popular, the critics point out, it is not the only contraceptive, nor even the only contraceptive pill, and the risks should be weighed against the risks of other contraceptive techniques.

Several of the authorities polled by the *Medical Tribune*, on the other hand, feel that the Wright committee's error lay in precisely the opposite direction—in not comparing the risks of Enovid and the risks of pregnancy in a more direct way. "The committee should have compared mortality of pregnant women and those having abortions with deaths apparently resulting from Enovid," said John Rock, one of Enovid's strongest supporters. "Instead, they limited their study to nonpregnant . . . women. I don't think they took into account that women using Enovid are avoiding the dangers of pregnacy and abortion." A similar view was expressed by Ann Southam, of Columbia University's College of Physicians and Surgeons, who said, "Even if we accept the mortality rate from Enovid, it is considerably smaller than the mortality rate from pregnancy. This is particularly true in a place like India where the standard types of contraception are not suitable." The majority of the dozen authorities interviewed felt that the report lacked an adequate statistical base; most felt that study of Enovid should continue; most of the doctors in the group indicated they would continue prescribing the drug.

Since the Wright report was issued, about 1 month ago, its critics have attempted to extract answers to their queries from the committee and from FDA, and to reopen a debate on Enovid on what they consider more valid grounds. So far they have had little luck. FDA Commissioner George Larrick answers, "we always look into such criticism," but says that FDA is standing by the report as written and expects no great shake-up.

The critics, however, are not entirely without allies. At the request of one of its members, Senator Ernest Gruening (D-Alaska), the subcommittee on reorganization and international organization of the Senate Government Operations Committee has been looking into the protests and trying to get authoritative answers to the questions raised. The subcommittee (which is better known as the Humphrey subcommittee and has displayed a special interest in drugs) is exploring, rather than investigating, the Enovid situation, soliciting additional scientific data and opinion. It is a delicate affair, not only because the propriety of legislative intervention in so technical a matter is uncertain, but because public alarms are so easily raised, and because the opinion of the Wright committee is sincerely respected. There is no attempt to undercut the Wright report; the sub-

committee is merely seeking to assure itself that the Wright committee had, and considered, all the relevant evidence.

In the meantime, however, while the critics are gathering material for what they hope will be their day in the limelight, the Wright report itself is being revised in a way that only increases the distance between the committee and its critics. When the Wright report appears in the *Journal of the American Medical Association*, on 7 September, the warning on greater risks of thromboembolism for Enovid users over 35 that appeared in the version released by the FDA will have been removed. "In making a final review," Wright said, "a small statistical error was discovered," and the committee now believes that no risk from Enovid exists.

—ELINOR LANGER

Announcements

Yale University this month will dedicate the Kline Geology Laboratory, a new facility for research and teaching in the **earth sciences**. It is the first unit of a science center made possible through a gift from C. M. Kline, board chairman of Smith, Kline, and French Laboratories, Philadelphia, Pa. The $3.5-million building includes laboratories, seminar rooms, offices, and space for a 62,000-volume library.

The University of California, Berkeley, has established a department of **entomology and parasitology**, to be headed by Ray F. Smith, entomology professor at the university. The department will include four divisions: biological control, entomology and acarology, invertebrate pathology, and parasitology. Three previously existing departments are combined in the new department.

Grants, Fellowships, and Awards

The National Science Foundation is administering the U.S. participation in this year's **NATO postdoctoral fellowships in science.** Approximately 45 fellowships will be offered in the mathematical, physical, biological, medical, and engineering sciences, sociology, psychology, geography, economics, and history and philosophy of science. The fellowships carry stipends of $5500 for a year, or $4125 for a 9-month academic term, plus travel and dependency allowances. Deadline: *18 October*. (Fellowship Office, NAS–NRC, 2101 Constitution Ave., NW, Washington 25)

The Jane Coffin Childs memorial fund for medical research is offering fellowships in the fundamental aspects of **neoplastic growth.** The awards help support postdoctoral research; they are open to foreign as well as U.S. citizens. Deadline for receipt of applications: *31 October*. (J. L. Lee, Jr., Childs Memorial Fund, 333 Cedar St., New Haven, Conn.)

Fellowships in **clinical pharmacology** are available at Hahnemann Medical College, Philadelphia, Pa. The 2-year training program will begin 1 July 1964 and will include both formal courses and multidisciplinary research. Applicants must hold an M.D. degree. Stipends will vary with the recipient's professional background. Deadline for applications: *31 October*. (J. H. Nodine, Hahnemann Medical College, 230 N. Broad St., Philadelphia)

Films

Highlights of Heart Research (15 minutes; black and white; free loan); causes, diagnosis, treatment, and prevention of heart disease; shows examples of research conducted or supported by the National Heart Institute. (Communicable Disease Center, Atlanta 22, Ga., Attn: Medical Audiovisual branch)

Fundamentals of the Nervous System (16 minutes; color; $5.75 rental). Structure and functions of the nervous system, and nature of nerve impulses operating to control learning processes, involuntary reflexes, and inhibitions.

The Community (11 minutes; color, No. 1944, $120; black and white, No. 1945, $60). Interrelationships of plants and animals in an ecological community and the function of each organism.

Bacteria (19 minutes; color, No. 1968, $210; black and white, No. 1969, $105). Basic characteristics of bacteria: structure, manner of feeding and reproduction; shows how they are classified and describes their functions.

These films are available from Encyclopaedia Britannica Films, Inc., 1150 Wilmette Ave., Wilmette, Ill.

Scientists in the News

Felix E. Browder, formerly professor of mathematics at Yale University, has been named professor of mathematics at the University of Chicago. He will spend the coming academic year on leave at the University of California, Berkeley, and at the Institute for Advanced Study, Princeton, and will become resident at the University of Chicago next July.

William Shockley has been named first Alexander M. Poniatoff professor of engineering science at Stanford University. He will act as professor-at-large in engineering and applied science, and will continue as consultant to the Shockley Laboratory of Clevite Transistor Co., Stanford Industrial Park.

John C. Frye, chief of the Illinois State Geological Survey, has been appointed professor of geology at the University of Illinois.

William K. Estes has received the Warren Medal for 1963 from the Society of Experimental Psychologists. He was cited for "development of a mathematical theory of learning . . . which has proved to be a powerful tool for analysing the role of stimulation in both human and animal learning."

The new chairman of the University of New Hampshire department of zoology is **Paul A. Wright**, associate professor at the university.

Marston Morse, professor emeritus of mathematics at Princeton University's Institute for Advanced Study, has been elected foreign correspondent of the Polish Academy of Sciences.

Samuel Loshaek, director of product development for the Borden Chemical Company, has been named director of research and development for the firm.

Lindsay Russell, former vice-president of Adams-Russell Co., Inc., has been named senior project engineer at Aerospace Research, Inc., in Boston.

Leon Kraintz, visiting professor of biology at the University of St. Thomas, Houston, Texas, has been appointed associate professor of oral biology at the University of British Columbia.