Letters

Contraceptives

In his useful and stimulating article entitled "Prognosis for the development of new chemical birth-control agents" (24 Oct., p. 468) Djerassi discusses two indivisibly related research efforts of the Center for Population Research at the National Institutes of Health: (i) the evaluation of medical effects and the mechanism of action of contraceptives in use, and (ii) the development of new methods of fertility regulation. Djerassi's comments are worthy of serious consideration coming as they do from a scientist with extensive experience in these areas but his argument is weakened by the consideration that it is based primarily on experience with steroid contraceptives which are known for their ubiquitous biologic effects in addition to their contraceptive effects. Studies supported by NIH and others lead many scientists to believe that these agents require special scrutiny simply because of their known effects on blood clotting, a multitude of metabolic functions, and animal carcinogenesis, among others.

One of the primary goals of agencies involved in contraceptive development, including the private nonprofit agencies and the government, as well as industry, is the development of chemical contraceptives with few, if any, biological effects other than fertility control. Indeed, many scientists and physicians hope that steroid contraceptive methods will no longer be in general use in several decades when a wider variety of relatively safe and effective methods with minimal side effects may be available.

Djerassi would undoubtedly agree that problems associated with population change are incredibly complex and subtle, interwoven with national and international issues, as well as the private behavior of individual couples. Solutions to these problems are also complex but it is clear that the effective control of fertility is an indispensable requisite to any solutions consistent with human dignity. Such control requires an effective technology, and government and nonprofit agencies wish to develop a wide variety of methods, including nonchemical methods such as new intrauterine devices and new methods of sterilization, as well as chemicals. Research on nonchemical methods has not been undertaken by the drug industry to any great extent. Government and nonprofit agencies are more interested in contraceptive methods than in products since it is not the ultimate purpose of these agencies to manufacture drugs to be sold for profit. The distinction is an important one: a good contraceptive method may not necessarily be a good product, from a commercial point of view.

Many informed citizens convinced of the need for new contraceptives would disagree with Djerassi's statement that "ample financial resources are being mobilized by government, industrial, and philanthropic sources." He refers to the Center for Population Research, a part of the National Institute of Child Health and Human Development at the National Institutes of Health, and its "annual multimillion dollar budget" for contraceptive development. The Center was established in August 1968 and in fiscal year 1969 it awarded about $5.6 million in contracts and grants for contraceptive development. A recent estimate established that all federal and nonprofit American agencies with major population programs contributed a total of $20 million to contraceptive development in the most recent 12-month period for which data were available. Unfortunately, comparable data from the drug industry are not available.

Djerassi mischaracterizes the Center's mandate to applied research as well as slighting the importance of fundamental research. He says that "under these circumstances" [the restrictive nature of the drug review process] "the newly organized NIH Center for Population Research may well stimulate interesting basic research in reproductive physiology but this will hardly result in development of a practical birth control agent before the next 3 billion human beings are added to the world's population." We hope that this prediction is incorrect and are encouraged by progress being made. Our mandate authorizes us to work with other agencies, private and nonprofit groups, as well as industry, to produce as rapidly as possible "birth control methods of all kinds" as directed in the President's Population Message to Congress of 18 July 1969.

Success in developing new methods before the end of this century will depend on the amount of domestic and foreign scientific and industrial resources which can be devoted to these fields as well as the ability to deal with issues of efficacy and safety, so ably discussed in Djerassi's article. Success will certainly depend on the contribution of scientists from many disciplines and countries including scientists from developing nations, who have already contributed significantly to these fields and who have the ability and interest to contribute much more. Significant IUD development, for instance, has been carried out in Latin America and Asia and certain new low dose oral contraceptives and contraceptive injections are now available overseas but not in the United States. This suggests that some foreign governments may not be as dependent on the decisions of the Food and Drug Administration as Djerassi suggests.

We feel that the Center for Population Research would make a significant contribution to contraceptive development even if it were restricted to "interesting basic research in reproductive physiology," which it is not. The success of oral contraceptives is based in a large part on several decades of "interesting" research in endocrinology undertaken in university laboratories and supported by nonprofit and government agencies before the concept of steroid contraception was developed. Contraceptive development is a continuing process and we need to obtain new information on reproductive processes in order to permit the development of new methods as requirements change with time.

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I certainly did not wish to downgrade the function of the Center for Population Research, with which I am in hearty agreement, or the importance of basic research, since the bulk of my past and present professional life is spent in this area. The point that I

wish to make is that factors completely outside the power of the Center for Population Research make conditions for the *application* of basic research findings in the fertility control field increasingly more difficult, and nothing in Corfman's letter contradicts this opinion.

I disagree with Corfman that only steroid contraceptives "require special scrutiny simply because of their known effects on blood clotting, a multitude of metabolic functions, and animal carcinogenesis, among others." I stated that irrespective of their chemical structure, all chemical birth control agents will be subjected to the type of detailed scrutiny outlined in my article; and it is preposterous to believe that the FDA or even any responsible investigator will pay less attention to carcinogenesis, blood clotting, or many other effects which may be caused by the continuous administration of any chemical agent for many years to a normal human population. Probably over 99 percent of all the chemical carcinogenic agents are not steroids, and I am convinced that our present attitude with respect to drug evaluation and eventual public use of any substance used in preventive medicine for long periods of time in normal populations will suffer from the difficulties which I have outlined.

Corfman states that "government and nonprofit agencies are more interested in contraceptive methods than in products since it is not the ultimate purpose of these agencies to manufacture drugs to be sold for profit." Within the context of my article, which specifically was limited to *chemical* birth control agents, no contraceptive method will have any effect in reducing population growth unless it is converted into a product which can be distributed and which can be used by people. In all technologically developed countries, with the exception of Eastern Europe, drugs for public use are developed by pharmaceutical companies and not by government or nonprofit agencies. Unless fundamental changes in drug development, manufacture, and distribution are effected, what is needed is intimate collaboration between industrial, government, and nonprofit agencies; and, if the urgency of the world population problem will stimulate such collaboration, then perhaps the prognosis is slightly less dismal than currently viewed by me.

Nestor (Letters, 26 Dec.) takes issue with my recommendation that an independent scientific body should be available to which rulings by the Food and Drug Administration on scientific matters dealing with clinical testing (which is a completely different matter from rulings on permission to market a compound) can be appealed. Nestor favors the present process which involves appeal through the courts. To me this seems completely unrealistic since very few research scientists or research organizations are prepared to go through court procedures in order to settle questions of scientific protocol and research procedure. My views are supported by the observation that virtually no court appeals have been made to such FDA decisions on clinical experimentation and that for all practical purposes such decisions are unappealable. I do, of course, agree that the courts are the right place to deal with matters of drugs that have passed the clinical evaluation phase and are introduced into open commerce.

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Alaska: A Climate for Cabbages

Frederick Lotspeich's article "Water pollution in Alaska: Present and future" (5 Dec., p. 1239) is in general an excellent overview of Alaska's situation, but he is guilty of repeating an old fallacy which people accept without thinking. He says, "Agriculture is unlikely ever to become important because of unfavorable climates and of Alaska's inability to compete with other areas of agricultural production." No evidence is presented for this statement, and it is nothing more than the perpetuation of the old belief that Alaska is a land of everlasting ice and snow.

The University of Alaska Agricultural Experiment Station has just completed a study of the potential for agricultural production within the state. We estimate the production potential of our class II and III land (classified according to the Soil Conservation Service) to be worth $386 million per year based on 1967 prices. We do not have the population to absorb that production, but we estimate the local market in 1985 will demand in excess of $50 million worth of agricultural products that we can and do produce here. Our population estimates are quite within the range reported by Lotspeich