

Senator NELSON. So what you are saying about it is that if a substantial dosage of a particular compound or chemical induces a certain effect, carcinoma, say, in an animal, that then you, at the least, must be concerned that it might do the same in the human species is that what you are saying?

Dr. LEGATOR. This would certainly be a warning to be taken quite seriously.

Mr. GORDON. Dr. Legator, just one question. This may have been asked before in different words. Are large doses given during a relatively brief period of time equivalent to the same quantity of test drug given in smaller doses but over a longer period of time?

Dr. LEGATOR. This depends on the agent. If we look at radiation here we have a cumulative effect and then we do say small doses given over a long period of time are essentially not too far different from a single large dose. With certain chemicals this doesn't necessarily follow. In the case of the oral contraceptives I don't know the answer to that question.

Now, I would like to discuss the area where information is almost nonexistent, not only for oral contraceptives, but also for drugs, food additives, pesticides, et cetera, the area of mutagenicity.

Here we are talking about an effect on the reproductive cells passed on from one generation to the other, and we may define mutagenicity as any inherited alteration in the genetic material. Such changes can lead to a wide range of abnormalities, mental retardation, physical and mental disease and all the other inherited weaknesses and debilities to which man is susceptible. The concern here is not only for the present generations, but for generations yet to come. The widespread use of oral contraceptives by women of child-bearing age, makes it especially imperative that the contraceptive steroids, singly and in combination be evaluated for metagenic effects. With the exception of limited cytogenetic studies, there is a void of experimental animal data in this area. The methodology needed to characterize potential mutagenic substances is of comparatively recent origin, and simply has not been applied to the evaluation of oral contraceptives.

Senator NELSON. To avoid any misunderstanding about it, you are not saying there is any evidence whatsoever of any mutagenic effect.

Dr. LEGATOR. Absolutely not.

Senator NELSON. What you are saying is we do not know and have not investigated?

Dr. LEGATOR. What I am saying here is that the methodologies in this area are of recent origin, most of them have been developed within the last year and they simply have not been applied to oral contraceptives the same as they have not been applied to food additives and pesticides and a number of drugs. They are just too recent. In fact, as I go on to point out there are a few, possibly three, laboratories in the country that are equipped to do comprehensive studies in this area of mutagenicity.

Mr. GORDON. Dr. Legator, with respect to these drugs, why are we concerned with the mutagenic effects?

Dr. LEGATOR. Simply because this is an agent here that is being used to a great extent by women of child-bearing age. This makes it extremely important to see if there is indeed any effect that can be passed on in the germ plasma of future generations. This is an extremely important area.