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LEGAL LIABILITY FOR GENETIC INJURIES FROM RADIATION*

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We know scientifically that ionizing radiation, including that from man-made sources, may cause genetic damage. This scientific knowledge has already acquired legal significance by serving as a basis for governmental recommendations and regulations controlling radiation exposure of workers and the general public.[1] In addition, a personal injury case in which a claim for genetic damage was made recently reached the trial stage.[2] With progressively increasing uses of nuclear energy and its resultant radiation risks the full legal impact of the genetic consequences of radiation exposure is an issue of present and great importance to lawyers. The purpose of this article is to analyze what genetic effects of irradiation of humans are legally significant. For example, if a Mongoloid child is born to the wife of the victim of an accidental exposure to ionizing radiation five years earlier, may legal damages be recovered?

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1. 10 C.F.R. Part 20 (1961) (AEC standards for protection against radiation). See also *Hearings on Radiation Protection Criteria and Standards: Their Basis and Use Before the Special Subcommittee on Radiation of the Joint Committee on Atomic Energy*, 86th Cong., 2d Sess. 614-22 (1960) (Federal Radiation Council Memorandum of May 13, 1960).

2. Troxell v. Bendix Corp., C.A. No. 12660, Fed. D.C. W.D. Mo., tried Jan. 28, 1963, deadlocked jury Feb. 14, 1963.

Mongolism has a naturally or spontaneously occurring incidence in the general population. It is also a congenital (present at birth) defect which could be induced by radiation exposure of either parent before conception or of the developing embryo at or immediately after conception. The mother and father probably have each had other exposures to radiation (*e.g.*, X-rays) in the course of medical and dental diagnostic procedures. Furthermore, both have been exposed to other mutagenetic agents throughout their lives. Although there is little or no affirmative evidence about their effects on man, conceivably such commonly used drugs as caffeine, nicotine, and aspirin might increase the incidence of Mongolism or other genetic or birth defects. In the light of these numerous other causal possibilities, if it is assumed that the operator of the radiation source was legally responsible for the exposure and would have a duty to compensate the father or, for that matter, a conceived but unborn child for damages resulting from the exposure, is the genetic injury one for which the law will provide compensation to either the parent or offspring?

The case of *Troxell v. Bendix Corp.* makes it clear that this is not an exercise in hypothetical questions.[3] In amended pleadings dated November 30, 1962, the plaintiff, a thirty-two year old woman, alleged permanent genetic damage resulting from periodic occupational exposure to gamma rays from a sealed 12.3-9.37 milli-curie cobalt-60 source over a period of approximately twenty-five months. If permanent genetic damage resulting from exposure to a source in the 10 milli-curie range already has been a major allegation in a suit, then it most likely will be the subject of serious controversy in suits involving large (50 rads or more) instantaneous exposures associated with criticality excursions (actual nuclear fission), nuclear reactor accidents, or multi-curie cesium-137, iridium-192, or cobalt-60 sources.

Primarily because of the difficult proof problems involved in genetic damage cases, it is our conclusion that unacceptably inequitable results will be reached if traditional methods of dealing with personal injury cases are used. If a way can be found to handle these problems in a scientifically and juridically more acceptable manner, it may prove to be a better method of handling medical-legal issues arising in other types of personal in-

3. *Ibid.*

jury cases as well. Although our recommendations here are limited to genetic injuries they suggest possibly more realistic solutions to the problems which other sources of personal injuries raise.

To understand the legal problems, however, a person first must become familiar with the complicated scientific vocabulary and theories of genetics. Then an analysis must be made of the effects of radiation on the factors determining human heredity. Lastly, we will consider those legal principles which will control recovery when these preconception injuries are in general indistinguishable from familiar pathological conditions which occur spontaneously in the general population. Of necessity, inter alia, this involves a careful analysis of rules concerning proof of causation in personal injury cases.

One general scientific conclusion of great legal significance, however, should be emphasized at the very beginning so that the scientific discussion will be put in proper perspective. *Low level or near background exposures probably are not legally significant in individual cases while larger short term* (acute) *exposures may be.* The legal consequences of possible genetic injury from radiation cannot be understood without an appreciation of this difference between low level occupational exposures and accidental acute (instantaneous or short term) and fairly high level exposures of an individual.

I. Scientific Concepts

Human genetics, the study of human inheritance, concerns the "inborn" physical and mental, normal and abnormal characteristics of human beings. It deals with both transmission and development of expression of hereditary factors and draws its data from experiments with plants, animals, and microbes and from anthropological, psychological, medical, and sociological investigations of humans.

A. Fundamentals of Genetics

The human body is made up of many millions of units called cells. The cell can be observed under the microscope and is comprised of a central portion called the nucleus and an outer area called cytoplasm. No matter where cells are found, in skin, the bones of the middle ear, or in the brain, they consist of the same

material, a nucleus and cytoplasm. Furthermore, in general, the nuclear substance of every cell, whether it be skin, brain, smooth muscle of the intestinal wall, or a white blood cell, is identical. For genetic purposes the most important cells, however, are those which control the inheritance of offspring and are produced in the gonads. The mature reproductive or germ cell of the male is called a sperm, and that of the female is called an egg or ovum. Mature germ cells, whether male or female, are called *gametes*. The fertilized egg formed by the union of the sperm and ovum is called a *zygote* and the embryo develops from the zygote.

It has been established for over a century that the nuclear portions (as distinguished from the cytoplasm) of the father's sperm and mother's egg carry the principal factors influencing heredity.[4] The nucleus of the cell contains the chromosomes on which genes are located. Chromosomes are visible under the microscope but genes are not. These chromosomes with their genic components are the primary determiners of human heredity and are chemically comprised of protein and a substance called DNA (deoxyribonucleic acid). This DNA, which has a complex spiral-like chemical structure, is considered to be the actual hereditary material.

In ordinary cell division which is called *mitosis*, the cell divides by a process in which the chromosomes in each dividing nucleus duplicate themselves. Subsequently each original chromosome separates from its newly formed duplicate, forming two identical nuclei.[5]

Scientists now believe that the human cell contains 46 chro-

4. The egg is much larger than the sperm, the egg having a great amount of cytoplasm and the sperm having very, very little. Their nuclei are equal in size and the hereditary influences of mother and father are about equal. See STERN, PRINCIPLES OF HUMAN GENETICS 7-13 (2d ed. 1960) [hereinafter cited as STERN].

5. "It seems highly probable that genes consist of chemical substances, called deoxyribonucleic acid (DNA), which are typically found only in chromosomes. . . . Within the cells each specific DNA compound is able to reproduce, i.e., to make more of itself during growth and chromosomal replication; to undergo occasional changes — *mutations* — and then reproduce itself in changed form; and to participate in the biochemical reactions which are the basis of the functioning and development of the individual cells and of the whole body. Just as a man is not simply defined by the chemical elements of which his body is composed but rather by their complex organization and dynamic interaction, so the biological term gene refers to the role which the DNA molecules play in the life of an organism.

"DNA molecules are long chains of molecular subunits and it is still not clear whether each gene consists of a specific DNA molecule, separable from all others, or whether two or more genes are part of a single DNA molecule." *Id.* at 28.

mosomes which are comprised of 23 pairs. As to 22 of these pairs, the chromosomes in each pair have the same size, shape, and staining characteristics under the microscope. One of the members of each pair has been contributed by the father and the other by the mother of the individual. Each of these 22 pairs are called *homologous* chromosomes, and one chromosome of the pair is called the homolog of the other member of the pair. These 22 pairs of homologous chromosomes are called *autosomes*.[6] One additional pair of chromosomes which are not identical in size, shape, and staining characteristics are present and bring the total number of chromosomes up to 46. These are called the *X* and the *Y* chromosomes. Collectively these are called the sex chromosomes because they determine the sexual characteristics of the individual.

The differences between the *X* and *Y* chromosomes are observable under the microscope and they are involved in the phenomenon known as sex linkage which is discussed below. In humans the sex determiners are located on the *Y* chromosomes and are responsible for the development of the male sex. The normal human male has one *X* and one *Y* chromosome. The normal female has two *X* chromosomes.

The soundness and integrity of the human body and its physical and mental development seem to depend on the basic constancy of the chromosomal constitution, 22 pairs of autosomes and one *X* and one *Y* chromosome in the male and 22 pairs of autosomes and two *X* chromosomes in the female.

Normally the nuclei of the mature egg and sperm contribute the same number of chromosomes to the zygote. The gametes (mature egg or sperm cells) each contain 23 chromosomes, one chromosome of each of the 22 autosome pairs and 1 sex chromosome. This number of chromosomes is called the *haploid* number. The 46 chromosomes of a fertilized egg (22 pairs of autosomes and 2 sex chromosomes) constitute the *diploid* number. In the human ovary or testes the immature reproductive cells (also called stem cells in both male and female) contain 46 chro-

6. "The chromosomes of the billions of body cells are, however, not simply division products of the original chromosomes of egg and sperm. We must think of the reproduction of chromosomes as a process by which the original chromosome builds a copy of itself out of the materials present in the cell. This process takes place some time before the separation of sister chromosomes. The dual nature of each chromosome can be seen as soon as the chromosomes become visible in mitosis." *Id.* at 16. A few are so similar that a definite assignment of a partner is difficult. *Id.* at 21.

mosomes and divide by ordinary mitosis. At a given point in maturation these cells undergo a unique reduction division process called *meiosis* which results in mature gametes each having a haploid number (23) of chromosomes. Meiosis is a two-step process in which a premeiotic germ cell nucleus with a diploid number (46) of chromosomes forms 4 gamete nuclei with 23 chromosomes (the haploid number). In the male four mature gametes are formed from each germ cell which undergoes the two-step meiotic process. In the female, since abundant cytoplasm is a very essential component of a mature ovum, only one mature gamete (ovum) is formed from each germ cell going through the meiotic process. The other three nuclei which are formed degenerate and do not participate in any subsequent fertilization and zygote formation.[7] This is important because in the male all of the chromosomes including those which might carry undersirable hereditary material might find their way into the nuclei of mature gametes but only one-fourth might do so in the female.

It has been recognized that the genes are localized on the chromosomes in an orderly manner.[8] The number of genes in the human diploid number of chromosomes has been estimated at not less than 2,000 or more than 50,000 pairs with 10,000 pairs being a most likely number.[9] The numbers are estimated in pairs because it is generally concluded that homologous chromosomes contain similar genes at identical chromosomal locations called *loci*. A gene may have more than one form or variation. Different forms of a given gene at the identical location on homologous chromosomes (loci) are known as *alleles*.

The term *genotype* is used to indicate the genetic constitution, and *phenotype* the physical appearance of the individual. The phenotype is observable or can be measured chemically. The

7. For a full discussion of meiosis, see *id.* at 63-80.

8. *Id.* at 25-28.

9. "Estimates of number of genes in Drosophila have been based on counts of bands in the salivary gland chromosomes and on such indirect approaches as estimating (a) the average frequency of genic changes (mutations) of a single gene, and (b) that of the sum of all genes. The ratio b:a then gives an estimate of the total number of genes. This leads to estimates of from 5,000 to 15,000 for the haploid set of four chromosomes in Drosophila. Whatever the number, it can be assumed that the number of genes in the chromosome set of man is of the same general order of magnitude. . . .

"A human individual receives, from his parents, a complete assortment of all genic loci in two sets of chromosomes, those of the egg and the sperm. Thus, the cells of his body harbor two assortments of genes or assuming the correctness of the foregoing estimate, some 10,000 pairs." *Id.* at 29.

phenotype is not always an indication of the genotype because the genotype of a given individual is constant while the phenotype is potentially variable, it being the result of interaction between the genotype and the nongenetic environment of the individual. The term *phenocopy* is used to designate individuals whose phenotype under the influence of nongenetic agents has become like one normally caused by a specific genotype in the absence of such nongenetic agents. Individual attributes such as blue eyes, blond hair, or albinism, which the layman would call characteristics, are called *characters* or *traits* by geneticists. Characters or traits are derived from genic action and may be defined as observable biochemical, cellular, anatomical, physiological, or mental features of the developing or fully-developed individual.

Characters or traits are separated from the genes by at least one and, often, numerous intermediate steps. From studies of different organisms, particularly the mold *neurospora*, it has been determined that the genes control the processes of cellular metabolism and synthesis of proteins and other biochemical compounds.[10] Genic action is the result of the complex biochemical reactions between the genes and the nongenic material of the nucleus and cytoplasm, many of the reactions being influenced by simultaneous or contemporaneous reactions involving other genes or cytoplasmic elements. Interdependence is the essential feature of gene-controlled reactions and is responsible for the phenomena of penetrance, expressivity, and modification discussed below.[11]

These concepts lead to two general conclusions: (1) that no simple connection exists between a single gene and most observable characters (characteristics to the nongeneticist) of the developed human; and (2) that a single gene, by being part of a network of reactions, will frequently influence more than one

10. See generally, HALDANE, HUMAN BIOCHEMICAL GENETICS (1954); WAGNER AND MITCHELL, GENETICS AND METABOLISM (1955).

11. "It may well be that the thousands of genes present in each nucleus are active in every cell, but in qualitatively or quantitatively different fashion. The specific activity may be determined by the different cellular environments in which the genes find themselves, and by interaction between genes and different substrates, may become enhanced and more manifold. On the other hand, quantitative differences in genic action within different tissues may be so great that some groups of genes are more or less inactive at one stage of differentiation, but are called into action if differentiation has proceeded far enough to provide them with suitable substrates with which to react. The assumption of continuous action of all genes at all times comes nearer to the truth than does the assumption of restricted activities of fractions of the genic set." STERN 36.

character. Consequently, if a character depends on many genes, changes in any one gene may result in a change in the character. For example, some harmful characters such as *retinitis pigmentosa*, an eye disease resulting in blindness, can be the result of any one of three abnormal genes. The determination of which of the genes is involved cannot be made by medical examination of an afflicted individual.[12]

Generally speaking, alleles (different forms of a given gene at the identical location on homologous chromosomes) at the same locus determine the appearance of similar traits. Differences among alleles appear to be of another order than those among genes, genes at different loci being comparable to the species of a biological system and its alleles to the varieties of that species. An individual is classified as *homozygous* for a given trait if the two alleles at the given locus are alike. If they are different he is classified as *heterozygous*.

These alleles may be related one to another in the order of dominance and recessiveness, codominance and intermediateness. The dominance (or recessiveness, *etc.*) of an allele is determined by the expression of the allele-governed trait in the heterozygote. Abnormal conditions which are caused by the presence of a single allele and result in an appreciable observable trait in the heterozygote are called dominants even if the homozygous condition for the abnormal gene is unknown or, if known, is identical with or more extreme than the heterozygous condition. Recessive traits are observable only in homozygotes, those who have received the abnormal or recessive allele from each of their parents. Intermediateness describes a character which is expressed in the heterozygote as one somewhere in varying degrees between the two homozygotes, with the limit between intermediateness and dominance or recessiveness not being sharp. Where the characters of each homozygote show up independently in the heterozygote then codominance exists. (This is rare for anatomical or observable structural traits but characteristic of the gene-controlled chemical substances which characterize the *A* and *B* blood groups.) Since most genes have multiple effects a gene can be dominant in regard to one effect and recessive or intermediate in regard to another.[13]

12. See also *id.* at 39-40 for further discussion which illustrates the various diseases which are the result of impaired formation of fibrin in blood clotting, as another example of a series of complicated mechanisms leading to one defect — impaired clotting of blood.

13. "In the final analysis, all genetic differences among human beings must

The genetic background provided by other genes is important in the study of the effects of gene action not only with regard to expression (dominance, recessivity) but also with regard to the effect of one gene on several processes or traits (pleiotropism) and to the complex connections between a given gene and an observable character (characteristic). There are many genes whose effect on development seems to be constant under all known circumstances, but there are also many others whose effects are variable. Since the gene and its effect are related only indirectly, a change anywhere along the network of interconnections may lead to a change in the expression of the gene, that is, to variable consequences of a constant gene. A genotype which may or may not produce a given trait because of varying conditions in its environment is defined as being incompletely penetrant, with penetrance being quantitatively expressed in terms of the percentage of all those who show the trait. These varying environmental conditions include the other genes of the two genic sets with which it is associated in the nucleus of the cell of a developing and aging individual, the cytoplasm, the maternal body from conception to parturition, and the external physical world from birth to death.[14] Penetrance affects not only heterozygously dominant genes but also dominant or recessive homozygous genotypes. Variation in phenotype can be manifest by penetrance (expression or no expression) or *variable expressivity* which is the degree of severity of expression often forming a continuous series from extreme expression to no expression.[15] Whenever the effects of a given genotype (established by pedigree) are variable, it can be assumed that both environment and genetic backgrounds have significant influences on penetrance and expressivity. The spe-

be produced by differences in the physiological process of their cells. Since it is assumed that genes produce their effects by chemical interaction with other cellular constituents, the study of genic action leads to a study of biochemistry. . . . [B]ut often the chemical basis of phenotype differences is far removed from the easily observable trait and special studies are required for its determination. *Id.* at 52-53. See also *id.* at 60-61.

14. "A dominant gene with phenotypic expression in all individuals who carry it has 100 per cent penetrance; one expressed in only half the individuals 50 per cent. To determine the penetrance of a specific gene, we must know the number of carriers who do not show its effect as well as the number who do. A method for such determination consists of counting the numbers of affected and unaffected parental pairs in whose progeny the incompletely penetrant gene expresses itself." *Id.* at 290-91.

15. "However, it should not be assumed that similar phenotypes, different only in degree, are always due to variable expressivity of the same gene. . . . Only when the expression of a rare trait varies in the same pedigree can we be reasonably certain that we are dealing with variable expressivity of a single gene." *Id.* at 297.

cific gene or genes primarily responsible for the appearance *vel non* of a trait are referred to as main genes and the rest are their genetic background.[16]

The genes in the process of passing from one generation to another through gamete formation by meiosis (reduction division) in general obey two laws, *segregation* and *independent assortment.* Segregation refers to the separation of alleles into separate gametes as part of the process of separation and subsequent division of the homologous chromosomes in meiosis. Independent assortment refers to the assortment of alleles mainly controlling one characteristic (such as hair color) from those controlling another (such as eye color), independently of each other during meiosis and gamete formation. Genes do not assort independently if they are linked, the term for this phenomenon being called *linkage.* Genes, as has been particularly well demonstrated in experimental animals, can be arranged into linkage groups which in general correspond to the chromosomal pairs. In theory there should be a linkage group for every pair of chromosomes. In actual meiosis, however, another phenomenon known as crossing-over takes place allowing some assortment of the alleles in a given linkage group. By this process homologous segments of paired maternal and paternal chromosomes undergo exchange. The assortment of genes in a linkage group resulting from crossing over is less frequent than that due to independent assortment of unlinked genes, although the frequencies approach each other the farther that two genes are separated in a given linkage group.[17]

Phenotypes (observable physical characteristics as contrasted with genetic characteristics) of two individuals may differ so that the phenotype of one can be regarded as normal and that of the other as abnormal, or the phenotype of both may be a variant of either normal or abnormal traits. Persons afflicted with a given abnormality may be genetically distinguished from normal persons by the difference of a pair of alleles at a single locus or in a polygenic trait by differences between the alleles at any one of a number of loci.

Traits based on genes located on the sex chromosomes are

16. For a discussion of modifiers which play an important role in expressivity and penetrance, see *id.* at 310-16. See also *id.* at 316-22 for a thorough discussion of sex-limited and sex-controlled traits, both of which are pertinent to the overall picture of expressivity and penetrance.

17. See *id.* at 245-88 for a full discussion of linkage and crossing over. See also *id.* at 67-73.

called sex-linked and are transmitted by sex-linked inheritance.[18] All definitely known human sex-linked traits are dependent on genes located on the *X*-chromosome.[19] Since the female has two *X*-chromosomes she may be either homozygous or heterozygous for the *X*-linked alleles. Since the male has only one *X*-chromosome and consequently has *X*-linked alleles on only one chromosome he is called *hemizygous* for the single allele of his *X*-linked genes. (It has no comparable allele on a homologous chromosome.) The *X*-linked alleles may be either dominant or recessive, but their effect will show up in the male in the event that they are present regardless of their dominance because the male has no corresponding allele which might be dominant and cover up a recessive allele. Most of the *X*-linked abnormal traits are of the recessive variety with the males being predominantly affected and the females being the carrier. This is illustrated by red-green color-blindness.[20] Some *X*-linked traits are dominant in which case half of the offspring of females carrying abnormal genes and all of the female offspring of males carrying abnormal genes will have the abnormality.

Harmful hereditary traits may be transmitted by either simple or sex-linked single factor inheritance or by polygenic inheritance. Detection of the traits is complicated by such factors as penetrance, expression, and modification. Consequently, some of the pedigree of the individual must be known if a determination is to be made as to whether or not an abnormal trait in a given individual is even hereditary, much less whether it is the result of any of the above modes of transmission from an affected ancestor on the one hand or of spontaneous or induced mutation in the father and/or mother on the other. The pedigree is the family tree of the individual (which generally is represented diagrammatically by the geneticist) and indicates the individual and his affected family and kindred and their relations to the affected individual and each other. By the use of statistics the geneticist can determine the probabilities of (1) a genetic basis for a given abnormal character, (2) the particular mode, including penetrance, of inheritance for the character, and (3) the probability of the character being the result of a

18. The X and Y chromosomes in the human differ in size and staining characteristics and it can be expected that the two sexes (male XY, female XX) are not equivalent with respect to the genes located thereon. For a full discussion of sex linkage see *id.* at 218-42.

19. See *id.* at 219-22 for a discussion of the question of Y linkage.

20. See *id.* at 222-32 for a full discussion of color blindness.

mutation in the germ cells of the immediate parents. By means of the ratios of abnormal offspring in the pedigree and the known or assumed calculated frequencies of alleles for given traits, these determinations can be made after application of certain correction factors.[21]

Marriages between relatives are defined as consanguineous marriages. Children from consanguineous marriages are more frequently homozygous for various alleles than are children from other marriages because closely related individuals (those arising from a common ancestor) have a higher chance of carrying the same alleles than less closely related persons.[22]

Before discussion of the mutational process it should be pointed out that different genes affect the viability (ability to survive) of an organism in different ways and in varying degrees from better-than-normal through normal and on to subnormal viability.[23] Certain alleles produce such severe disabilities and impairments that the affected individual's viability is reduced so far that he fails to survive until the reproductive age is reached, thereby eliminating further transfer of the allele. Such alleles are termed lethal or sublethal and may be either dominant or recessive. A lethal allele is defined as one which does not permit survival of an embryo or infant, and sublethals are defined as alleles leading to death at the latest before the reproductive age is reached. The effects of lethal and sublethal alleles can be changed by penetrance and expressivity.[24]

Because many detrimental or even lethal alleles are completely recessive or are only completely expressed in the homozygous condition, the full detrimental effect of their presence is not phenotypically expressed (manifested in an observable physical trait) in any one generation. These hidden detrimental or lethal alleles are described in terms of lethal or detrimental

21. See *id.* at 81-87, 127-73, 424-44 for a full discussion of probability, genetic ratios, the Hardy-Weinberg Law, and sex ratios.

22. *Id.* at 369-97 for a full discussion of consanguinity.

23. The criterion defining viability is average life span attained under normal conditions by individuals of a given genotype. For a discussion of viability and lethal and sublethal genes see STERN 113-26. See also U.N. SCIENTIFIC COMMITTEE ON THE EFFECTS OF ATOMIC RADIATION, *Report*, U.N. GEN. ASS. OFF. REC. 17th Sess., Supp. No. 16, at 87-89 (A/5216) (1962) [hereinafter cited as U.N. SCIENTIFIC COMMITTEE], for a discussion of relative genetic fitness, the role of heredity in premature death, and a discussion of lethal and detrimental equivalents.

24. Some lethal or sublethal alleles are dominant in that they produce an effect in the heterozygote (the effect is present but not lethal) but produce their lethality only in the homozygous condition. See STERN 117-19.

equivalents. A lethal equivalent is defined as a group of mutant genes of such number which if dispersed in different individuals will cause one death, on the average, the death being attributable to the homozygous condition of the lethal equivalent. Studies show that on the average human beings carry from 2 to 4 lethal and an additional 2 to 4 detrimental equivalents which are or may be expressed in homozygotes before the age of 20 to 30.[25] The role of lethal and detrimental alleles in the maternal and paternal gametes and their effect on the production of relative or absolute sterility, abortions, stillbirths, and neonatal (within three weeks of birth) deaths has not been adequately determined, but there is evidence from experimental animals that genetic mechanisms contribute to the incidence of all of these conditions. This contribution can only be studied and ascertained with difficulty because the affected zygotes, embryos, fetuses, or neonates produce no offspring.

B. Mutations

1. General Considerations

Gene mutation is the process by which an allele already in existence with a certain composition is transformed into a new allele.[26] It occurs both in somatic (body) and germ (reproductive) cells. Germ cell mutations are the only type which are transmitted to succeeding generations and are our concern here. The appearance of a trait, subsequently inherited in a member of a family in which the trait was unknown suggests the possibility of a mutation. This suggestion is not always justified. If the trait is based on either an autosomal or sex-linked dominant allele which is fully penetrant, the first appearance of the trait denotes the origin of the new allele (mutation) in the immediately preceding generation. However, if there is incomplete penetrance or autosomal or *X*-linked recessiveness of the allele then the phenotypic expression of the allele might have last occurred at a point in the pedigree far removed from the present case. These factors can be ruled out only by the presence of adequate pedigree data, showing not only parents, more remote ancestors, brothers, or sisters but also *off-*

25. U.N. SCIENTIFIC COMMITTEE 87. Detrimental equivalents are defined in the same manner as lethal equivalents but the criterion is that of a visible recessive defect rather than death.

26. STERN 445.

spring, from which the statistical probabilities of the expressivity and mode of transmission of the allele can be calculated.

In organisms which have been subjected to genetic experiments gene mutations can be detected and characterized directly quite readily by breeding experiments and procedures. In man only mutations to dominant autosomal or sex-linked alleles or to sex-linked recessive alleles can be recognized, and exact determination and characterization requires sufficient pedigree data from which statistical probabilities can be calculated.[27]

In man the frequencies of specific mutations have been estimated by two different methods. The direct method, which is primarily applicable to dominant mutations, is based on a census of the frequency of children with well-known dominant traits who are born to parents without these traits. This estimate assumes that there is always full penetrance, that the trait is never produced by recessive alleles, that the trait is never produced by nongenetic agents, and that dominant alleles at only one locus produce the trait.[28] Validity of these assumptions has not been verified in most cases and full proof of their correctness may be difficult to obtain.[29] Furthermore it is known that few mutations are completely dominant, although the disease or defect ordinarily is considered to be caused by dominant alleles.

Mutation frequency (mutation rate) also can be estimated by the indirect method. This method is based on the assumptions: (1) that alleles causing abnormalities reduce reproductive fitness and are not transmitted to as many individuals as normal alleles, leading to a decreased frequency of abnormal alleles from one generation to another and tending to eliminate them from the population altogether; (2) that the progressively diminishing store of abnormal alleles is constantly replenished by recurrent mutations from normal to abnormal, making the mutation rate balance the rate of loss caused by decreased reproductive fitness.[30] The mutation rate of abnormal alleles is then

27. *Id.* at 446.
28. *Id.* at 450.
29. *Ibid.*
30. *Id.* at 451-63. Reproductive fitness is the likelihood of an individual with a given set of alleles to reproduce and transmit the alleles as compared with the likelihood in the general average population. Normal fitness is one. Most abnormal traits decrease the likelihood that the individual possessing them will have an average number of children, because of early mortality, reduced prospects of marriage, or decreased number of children produced by the sexually matured married affected individual.

The controversial issue among geneticists concerns the effect on reproductive

estimated from the frequency of the abnormality associated with the allele and the reproductive fitness of the individual carrying the allele in the case of dominant abnormal mutations. This method can also be adapted to estimate rates for recessive autosomal and *X*-linked mutations. However, these adaptations are valid only in those cases where the allele does not increase or decrease reproductive fitness in the heterozygote which we know is the exception rather than the rule.[31]

In addition to gene mutation new inherited traits can result from changes in the quantity and/or the arrangement of the chromosomal material in the nucleus of the sperm and egg or their precursors. The proper cellular and developmental processes depend on both the presence and harmonious interaction of the necessary alleles.[32] This presence and arrangement can be affected by abnormalities in the division or the distribution of the chromosomes or chromosomal sections during cellular division by mitosis or meiosis. Experimental studies of plants and animals have shown that development does not proceed normally in the presence of abnormal chromosomal types. Modern methods of studying human chromosomes are opening up a new avenue of investigation and discovery of the causal relation between chromosomal abnormalities and observable congenital and hereditary human abnormalities.[33] These modern methods employ what are called cytological techniques in which the cells, chromosomal pairs, and individual chromosomes are observed and studied microscopically. The study of the relation between

fitness of the heterozygous condition of a given allele which is detrimental or lethal when homozygous.

31. "The relationship between mutation, genetic fitness, and the prevalence of hereditary disabilities is concisely expressed by the principle which holds that each mutation, whether fully lethal or slightly detrimental, will on the average result in the death of a descendant or in a failure to reproduce. The more genetically unfit of these mutations, as for instance dominant lethals, will be eliminated quickly. . . .

"Genetic damage can affect the phenotype of individuals in either the homozygous or heterozygous states. It is known that few dominant diseases and defects are completely dominant and it is becoming increasingly clear that many recessive traits may not be, in fact, completely recessive. This partial dominance can reflect on the genetic fitness of heterozygotes. . . .

"One of the advances in human population genetics has been the discovery of several balanced polymorphic systems. . . . Such systems arise when a gene confers reduced genetic fitness in some circumstances and increased fitness in others. The increase in fitness may be a consequence of a shift in the macro- or micro-environment or it may be a consequence of heterozygosity as contrasted with homozygosity. The role of mutation in supporting the frequency of polymorphic systems is minor." U.N. SCIENTIFIC COMMITTEE 88. See also *id.* at 88-89.

32. See STERN 467-78 for a full discussion of chromosomal changes and abnormalities.

33. U.N. SCIENTIFIC COMMITTEE 84.

genetic effects and observable chromosomal features is called cytogenetics.

2. Genetically Influenced Human Abnormalities and Defects

Human diseases and defects such as hemophilia, red-green color blindness, total color blindness, phenylketonuria, albinism, microcephalic idiocy, infantile and juvenile idiocy accompanied by blindness, muscular dystrophy, deaf-mutism, certain forms of dwarfism (achondroplasia), connective tissue disorders (arachnodactyly-Marfan's syndrome), Huntington's chorea, Mongolism, various forms of mental retardation, diabetes mellitus, and schizophrenia, to name a few, have some genetic or hereditary component or involve alterations in the chromosomal number or arrangement in affected individuals.

In man the size of the burden of hereditary diseases and defects is estimated from the frequencies of:

(a) miscarriages, stillbirths, and neonatal deaths

(b) infertility

(c) hereditary diseases and defects

(d) detrimental deviations from normal in continuously varying degree of such traits as intelligence, life span, and resistance to disease.[34]

Deleterious hereditary traits may be the result of undesirable alleles or chromosomal aberrations (abnormalities). The prevalence of abnormal hereditary phenotypes in the population does not provide a complete estimate of the amount of hereditary damage which is present since in some instances the phenotype is completely or partially masked in the heterozygote (or even homozygote) or has such differences in expressions between homozygote and heterozygote that the total harm cannot be described in simple terms.

Data on the prevalence of hereditary diseases and defects presently are restricted to that collected by geneticists for special purposes in limited populations from a small number of countries. The data from Northern Ireland is the rseult of the most comprehensive survey yet undertaken and has served as

34. U.N. GEN. ASS. OFF. REC. 13th Sess., Supp. No. 17 (A/3838) (1958). See also STEVENSON, EFFECT OF RADIATION ON HUMAN HEREDITY, U.N. Doc. No. A/AC.82/G/R.58 (1957).

the basis for estimating the over-all incidences of many diseases and defects.[35] It has been estimated that readily detected hereditary diseases and defects occur in approximately four percent of the population. These have been classified in four categories according to the role which mutation is considered to play in maintaining their frequency.[36]

The first category includes harmful traits whose prevalence is determined primarily by point (individual gene) mutations or by cytologically demonstrable chromosomal aberrations produced by recurrent mutation. It is broken down into two subcategories based on (a) point mutations (category I a), and (b) chromosomal aberrations (category I b).

Several hundred traits determined by single gene substitution (point mutation) autosomal dominant and *X*-linked and autosomal recessive alleles have been tentatively identified. The majority of the traits associated with dominant alleles are sufficiently mild in their effects to be transmitted through several generations. Those recognized defects associated with recessive alleles are extremely severe and are with few exceptions lethal in the genetic sense, having a reproductive fitness approximating zero. Since the dominant defects show up in the heterozygotes, about 70 percent of the detected and characterized specific defects attributed to point mutations are determined by dominant alleles. Because of the above-noted difference in reproductive fitness, about 90 percent of persons showing *monomeric* (single gene) defects have defects determined by a dominant allele. However, in terms of gene frequency and, therefore, in terms of production by mutation, genes for recessive harmful traits must outnumber those for dominant traits in a given population.[37] Furthermore, in the human population there are many hundreds of traits which existing evidence suggests come by a recessive mode of inheritance, but they are so rare that adequate evidence for proof of mode of inheritance is lacking. It is very likely that many of these are homozygous expressions of recessive alleles and that they account in total for the greatest contribution to the frequency of detrimental traits in populations.[38] Furthermore, since the data from which the prevalence of the abnormalities in the subcategory are estimated was

35. U.N. SCIENTIFIC COMMITTEE 85.
36. *Id.* at 86.
37. *Ibid.*
38. *Id.* at 85.

collected for special purposes and did not include defects in which the genetic component was equivocal, the over-all size of the subcategory has not yet been fully determined. Finally, since many hereditary defects which are slight, but nevertheless of importance to humans, are not easily recognized in other species, generalizations based on the results of experiments with other organisms entail considerabe uncertainties.[39]

As a result of improved techniques in human cytogenetics direct evidence has been acquired that congenital and other physical defects are sometimes caused by chromosomal aberrations.[40] Since there is often significant variation in the clinical severity of defects caused by chromosomal aberrations, all the clinical aspects of some specific defects are yet to be described. These defects can be the result of anomalies in the numbers of autosomes or sex-chromosomes or can be attributable to chromosomal rearrangements. The best known defect in humans associated with chromosomal abnormalities is Mongolism (Down's syndrome) which is associated with an extra chromosome number 21 (Denver Convention).[41] There are, however, many unanswered questions regarding even Mongolism.[42] Klinefelter's and Turner's syndromes are associated with anomalies in the number of sex-chromosomes.[43] Mental retardation, sterility, stillbirths, and miscarriages are the gross abnormalities with which chromosomal aberrations (defects in numbers of autosomes or sex chromosomes or rearrangements) most usually are associated. Most of these aberrations can be detected by cytological

39. *Id.* at 86.
40. *Ibid.*
41. *Ibid.*
42. "Our knowledge of other organisms indicates that a tendency toward nondisjunction of a chromosome may be inherited — a phenomenon which could account for the slight increase in Mongols among the relatives of affected individuals. But it is not yet clear why the normal relatives of affected individuals more often than unrelated ones have a simian fold or an enlarged palmar angle. . . . And why do the fathers of Mongols have a large palmar angle less frequently than the mothers and sibs? Answers to these questions will undoubtedly be forthcoming from the intense studies of human cytogenetics which are now pursued in many laboratories." STERN 473-74.
43. Turner's syndrome is a disease occurring in phenotypic females and is characterized by ovarian dysgenesis (nonformation), sterility, infantile stature and secondary sex characteristics (breasts, genitals, uterus), a web neck, and a higher than normal incidence of mental retardation. The individual with Turner's syndrome has only one X chromosome and no Y chromosome. See NELSON, TEXTBOOK OF PEDIATRICS 1198-99 (7th ed. 1959). Klinefelter's syndrome is a disease occurring in males and is characterized by small testes, azoospermia and sterility, elevated urinary gonadotrophins, testicular dysgenesis, sometimes large breast development after puberty, possible varying degrees of eunuchoidism, and a higher incidence of mental retardation. The individual with Klinefelter's syndrome has two X and one Y chromosomes. See *id.* at 1197.

studies of the white blood cells, buccal mucosal cells, or other tissues of the affected individuals.[44] As noted above, the frequency of these defects is maintained by mutation. More than half are anomalies in number of chromosomes with the rest being associated with intrachromosome changes, translocations, or combinations of these with numerical changes.[45] Only a small fraction of these are transmitted to subsequent generations, but when they are transmitted they are transmitted as dominants.[46] Despite the newness of the research in cytogenetics, a general picture of the prevalence of these defective traits is emerging.[47]

The second full category (category II) includes developmental malformations whose mechanism of inheritance is poorly understood. Cleft palates, harelips, pyloric stenosis, and congenital heart defects are examples of category II defects. Environmental factors are influential in their etiology and the existence of a genetic component has not yet been established. The role of mutation in maintaining their frequency has not been ascertained.[48]

The third category (category III) includes serious "constitutional" disorders and encompasses schizophrenia, the manic-depressive psychosis, diabetes mellitus, pernicious anemia, and certain thyroid disorders. These diseases are common, are found throughout the world, have definite familial distribution, and maintain a high frequency despite their seriousness. It is generally agreed that a major genetic component exists in all of these disorders but simple modes of inheritance are not usually assumed.[49] The role of mutations in the maintenance of these disorders is also unclear. Category III disorders were estimated, albeit uncertainly, in 1958 to affect at least 1.5 per cent of all adults and schizophrenia alone has been estimated to occur in one per cent of the adult population.[50]

Category IV includes traits which are determined at single loci, just as are those of category I a. However, gene mutation is a most unlikely factor in maintenance of the trait. These in-

44. U.N. SCIENTIFIC COMMITTEE 86.
45. *Id.* at 86-87 and 101-02.
46. STERN 467-78.
47. U.N. SCIENTIFIC COMMITTEE 86.
48. *Id.* at 87.
63 (1960); STERN 580-84 (schizophrenia), and 295 (diabetes).
63 (1960); STERN 580-84 (chizophrenia), and 295 (diabetes).
49. *Ibid.* See also Edwards, *The Simulation of Mendelism*, 10 ACTA GENETICA.
50. U.N. SCIENTIFIC COMMITTEE 87.

clude such hereditary abnormal hemoglobin disorders as sickle-cell anemia and thallasemia and probably include fibrocystic disease of the pancreas.[51] Therefore, these traits probably are unimportant when dealing with genetic effects of exposure to radiation.

From the above discussion it becomes apparent that the nature of the genetic component, the mode of inheritance, and the role of mutation in the human diseases and defects with a hereditary or familial component is far from completely known and is still the subject of a great deal of investigation and speculation.[52] The most definitive conclusions can be drawn in those abnormalities associated with chromosomal aberrations which have been established cytogenetically, but even here much more remains to be determined.[53]

3. The Role of Radiation

In gene mutation the molecular structure of the DNA in question is changed, and this change results in continuation and reproduction of the new molecular structure.[54] Gene mutation in the egg and sperm cells or their precursors is the only way by which changes attributable to external agents are inheritable. External agents which are capable of producing mutations are called mutagens and they may be either physical or chemical. It is presumed that mutagens produce mutations only in cells on which they act directly, apparently by direct effect on their nuclei.

Mutagenic chemicals such as mustard gas, nitrogen, or sulfur-mustard compounds, formaldehyde, various alkaloids (drugs

51. The frequency of these traits tends to be high in localized areas of the world, e.g., sickle-cell anemia on the west coast of Africa and thallasemia along the Mediterranean Sea. Their localized high frequency is a consequence of the fact that each of the traits exists as a part of a system of balanced polymorphism in which because of the increased reproductive fitness of the heterozygous genotypes in certain geographical areas and environments, evolutionary selection pressures give the allele an advantage. Sickle-cell anemia, a disease which is fatal in homozygotes, provides an example of heterozygous advantage in genetic fitness. These heterozygous individuals have an increased resistance to malignant tertian malaria and a consequent selective advantage in a malarial environment. A change in environment such as movement from Africa to the United States might remove some traits from this category or render them extinct as a result of the loss of the evolutionary selection advantage. See *id.* at 87, 88, 89.

52. See generally, THE USE OF VITAL STATISTICS FOR GENETIC AND RADIATION STUDIES (U.N. Pub. Sale No. :61 XV118) for a further discussion of this subject.

53. See note 41 *supra* and accompanying text as one example.

54. STERN 482.

including colchicine and possibly morphine, codeine, caffeine, nicotine) and steroids (hormones such as cortisone or the estrogenic hormones) can cause mutation only in the cells that they penetrate.[55] The mutagenic effect of chemical mutagens in man remains open to question because chemicals that enter the human body undergo many changes and must cross many chemical and physical barriers before reaching the interior of cells.[56] The effect of these changes and barriers may or may not preclude or modify the action of the chemical mutagens.[57] In this connection caffeine accumulation in the reproductive tissues has been demonstrated.[58]

The principal physical agents are penetrating ionizing radiation, heat, and ultraviolet light. Of all of the mutagens, penetrating ionizing radiation is of particular importance because it is capable of penetrating *in unaltered form* into the reproductive tissues themselves and acting directly on the germ cells (sperm, egg, precursors) and their nuclear material. Although the mutagenic effect of radiation has never been demonstrated in humans, it has been clearly demonstrated in all experimental animals and since the genetic substance in the animals is the same as in man because the mechanism by which hereditary information is transmitted is basically the same in all forms of life, there is general scientific acceptance of the proposition that penetrating ionizing radiation is mutagenic in man.[59] The means by which radiation produces gene mutations and the details and mechanisms of the mutational process remain to be developed by those doing research in molecular biology.[60]

Gene mutations may be *spontaneous* or *induced.* Spontaneous mutations account for the frequencies of mutant alleles in the population and for the frequencies of hereditary diseases and defects which are maintained by mutation (categories I a and I b discussed above). The factors responsible for the occurrence of spontaneous mutations have not been completely determined or characterized. However, the general scientific assumption is that the natural background radiation to which mankind is ex-

55. *Id.* at 484.
56. *Id.* at 484. See also generally, SCHULL, MUTATIONS — SECOND CONFERENCE ON GENETICS (1962) [hereinafter cited as MUTATIONS].
57. MUTATIONS 157, 233-37.
58. *Id.* at 235.
59. U.N. SCIENTIFIC COMMITTEE 85.
60. There is evidence that radiation exerts its effect on the genes indirectly by producing highly reactive chemicals inside cells. STERN 485.

posed accounts for *not more than ten percent,* and probably less, of the spontaneous or naturally occurring gene mutation rate in man.[61] The extent to which man-made or man-delivered ionizing radiation increases this naturally occurring mutation rate and leads to the production of hereditary abnormalities will be the subject of the remainder of this discussion. These mutations are classified as induced rather than spontaneous.

Certain assumptions about radiation-induced mutations must be understood. Radiation is not specific for particular genes or groups of genes and it affects each gene independently.[62] Also, in considering the genetic effects of radiation, the presumption that mutations in general are deleterious to individuals and to the population is currently held to be justifiable.[63] Likewise, it is thought that mutant genes are usually recessive, and consequently the changed character resulting from the mutation seldom appears fully expressed in the first generation of offspring of the person who received the radiation and developed a radiation induced mutation in a germ cell.[64] Furthermore, because of the problems of penetrance and because a single gene usually affects several characters and characters are practically always affected by many genes, a deleterious mutation when viewed from the standpoint of a given individual may cause an amount of harm varying from death, or loss of ability to produce offspring, to a serious abnormality, to smaller handicaps which might tend to shorten life or reduce the number of children, to no harm at all.[65] From the standpoint of a given population or of society as a whole, rather than the individual, genetic damage is roughly directly proportional to the mutation rate.[66]

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61. See *id.* at 484-88 for a more complete discussion of spontaneous mutations.

62. *Id.* at 15. See also NATIONAL ACADEMY OF SCIENCE-NATIONAL RESEARCH COUNCIL, THE BIOLOGICAL EFFECTS OF ATOMIC RADIATION 11 (SUMMARY REPORT) (1956) [hereinafter cited as RESEARCH COUNCIL (1956)].

63. See STERN 503-05. "Since so many mutants are disadvantageous to their bearers, it is likely that each species builds up a genetic control system which reduces the frequency of mutations as much as is compatible with providing adaptive and evolutionary flexibility. If this is true, then an artificial increase of human mutation is undesirable even from an evolutionary viewpoint. Although mutations have been induced which are useful to man (for instance mutations in the mold penicillium have resulted in the production of a higher than normal amount of penicillin), they are very greatly outweighed by those which are unfavorable. If we wish to produce favorable mutations in man, we must pay a human cost in terms of numerous unfavorable mutations." *Id.* at 504-05. See also RESEARCH COUNCIL (1956) 14-15.

64. RESEARCH COUNCIL (1956) 16.

65. *Id.* at 20-22.

66. *Id.* at 3.

As was stated above, most information on radiation-induced mutations comes from mouse and fruit fly (Drosophila) experiments which *in general terms only* can be made applicable to man because of the fundamental similarity of the mutation process in all forms of life.[67] In humans, there is a general assumption that all radiation down to zero dose entails some risk or probability of producing mutations in a population. Studies on the fruit fly at more than fifty loci have indicated that acute exposures as low as 5 rads have a statistically significant mutagenic effect and that the dose-effect curve is directly and linearly proportional from lower to higher doses.[68] In bacteria (E. Coli) evidence of a straight line dose-effect relationship down to doses as low as 8.5 rads has been noted.[69] Consequently, the assumption of a linear dose-effect relationship down to a zero dose has been strengthened. Therefore all official bodies and groups have continued to accept the conclusion reached in 1956 that: (1) Any radiation dose, however small, can induce some mutations and hence not only is there no minimum amount of radiation dose which must be exceeded before any harmful mutations can occur, but also mildly larger doses of radiation produce more but not worse mutants. (2) Although many mutations do disturb normal embryonic growth, most mutations do not commonly result in monstrosities or freaks, the commonest being those with the smallest direct effect on any one generation — the slight detrimentals.[70]

Scientists also generally agree that the rate of delivery of ionizing radiation affects the mutation rate induced by a given dose. Low dose rates are about one-fourth to one-sixth as harmful as instantaneous or acute exposures for a given amount of

67. U.N. SCIENTIFIC COMMITTEE 92.

68. *Ibid.* See also, Glass and Ritterhoff, *Mutagenic Effect of a 5-r dose of X-rays in Drosophila Melanogaster*, 133 SCIENCE 1366 (1961). See *Hearings Before the Subcommittee on Research, Development, and Radiation of the Joint Committee on Atomic Energy*, 87th Cong., 2d Sess. 333-49 (1962). "In my own laboratory we recently completed a 3-year study of the mutation frequency produced by a dose of only 5 roentgen to the mature male and female germ cells, which is, I believe, the lowest dose studied for its mutagenic effect in any animal up to this time. Dominant mutations of a particular minute bristle type were studied, and a total of 1,360,948 individual flies descended from parents which had received a 5-roentgen dose of X-rays were scored." *Id.* at 338. (Testimony of Dr. H. Bentley Glass).

69. U.N. SCIENTIFIC COMMITTEE 92.

70. RESEARCH COUNCIL (1956) 15. See also NATIONAL ACADEMY OF SCIENCES-NATIONAL RESEARCH COUNCIL, THE BIOLOGICAL EFFECTS OF ATOMIC RADIATION 4 (SUMMARY REPORTS) (1960) [hereinafter cited as RESEARCH COUNCIL (1960)]; see also U.N. SCIENTIFIC COMMITTEE 92, 99. FEDERAL RADIATION COUNCIL, BACKGROUND MATERIAL FOR THE DEVELOPMENT OF RADIATION PROTECTION STANDARDS REPORT No. 16960.

radiation, although below certain dose rates no further reduction in mutation frequencies occurs.[71] Investigation has not yet elucidated the mechanism involved in this dose rate phenomenon but there is strong evidence that it is the mutation mechanism itself that is affected, quite likely by some kind of repair of premutational damage occurring at the lower dose rates.[72]

The retention or continuation of a mutant allele by the germ cells of a given individual is dependent upon the stage of *gametogenesis* (development of mature gametes from stem cells) at which the mutation occurs. If it occurs in a so-called stem cell (a germ cell that is very immature and which divides to form more stem cells as well as cells that go on to form mature gametes) it could be transmissible to the progeny of the individual throughout his or her reproductive life. If it occurs in the mature gamete it will be lost when that gamete is discharged. However, to preclude underestimating the potential harm produced by radiation exposure in a given population, geneticists assume that the mutant allele, once formed, is transmissible throughout the reproductive life of the individual.

Experimental studies have shown that natural (spontaneous) and induced rates of mutation vary markedly at different loci in various organisms.[73] They have further shown that the frequency of radiation-induced mutations can be influenced both by sex and the stage of gametogenesis at the time of exposure.[74] Species differ widely in their genetic sensitivity to radiation and while the general principles developed from experimental animals can be applied to man because of the fundamental similarity of the mutation processes in each, no specific findings such as the specific dose required to double the spontaneous mutation rate at a given locus in an experimental animal can be applied to humans.[75]

The concept of a "doubling dose" for a particular mutation has been given a great emphasis. It means that dose of radiation which will increase the mutation rate to double the spontaneous rate. From the "doubling dose" a prediction of the

71. See U.N. SCIENTIFIC COMMITTEE 92-93 and publications referred to in items 119, 121, and 123-27 of the Bibliography on Hereditary Effects (A/5216) (1962).

72. *Id.* at 93-94 (particularly materials dealing with repair of premutational damage).

73. *Id.* at 94.

74. *Ibid.* See also testimony of Dr. Glass cited in note 68 *supra*.

75. U.N. SCIENTIFIC COMMITTEE 94.

phenotypic effect of an increase in mutation rate can be calculated, since the number of affected persons arising as a consequence of a doubling dose delivered in one generation, is equal to the number of affected persons normally present in any one generation as a result of recurrent spontaneous mutations.[76] Such a concept would be helpful because by use of it whole classes of mutations could be handled as a unit in the absence of any information about the number of loci involved or their individual mutation rates.[77] Sufficient information is not now available to calculate with a useful degree of accuracy a representative dose which would double the mutation rate in general. Nor is it now possible to make direct predictions of the quantitative or qualitative effects of such dose on the population.[78]

At the present time the doubling dose can be most accurately estimated for those severe defects maintained by recurrent point mutation (category I a).[79] It is most probably about 50 rad for both sexes in cases of instantaneous or short-term exposure and about 200 rad for long-term low intensity exposure. A permanent doubling of the mutation rate would *ultimately* double the prevalence of these defects, but not in the next generation unless the mutation was truly and completely dominant.[80]

It has been known for many years that radiation can cause small and extensive chromosome changes and rearrangements in experimental plants and animals.[81] Studies of human cells grown in tissue culture have shown that doses as low as 25 roentgens will cause detectable chromosome breakage in a significant proportion of the cells.[82] In eight men accidentally exposed to mixed gamma ray and fission neutrons, chromosome aberration in the circulating white blood cells persisted for 2½ to 3 years after exposure.[83] These aberrations resulted in cells with chromosome counts different from 46 in those with both high and low exposure. Grossly altered chromosomes were noted in the more highly exposed cases.[84] No measure of the sensitiv-

76. *Id.* at 100.
77. *Ibid.*
78. *Id.* at 101. See particularly paragraphs 153-156 for a discussion of the usefulness of the doubling dose concept. See also MUTATIONS 223.
79. U.N. SCIENTIFIC COMMITTEE 101.
80. *Ibid.* See also STEIN 498-99.
81. U.N. SCIENTIFIC COMMITTEE 95.
82. *Id.* at 133.
83. *Ibid.*
84. *Ibid.*

ity of germ cells has yet been made.[85] However, Stern has summarized the genetic effects to be expected in the germ cells of man as follows:

> (1) Many aberrations produced in stem cells (early immature gametes) will be eliminated before meiosis occurs.
>
> (2) Many aberrations induced in germ cells which are ready for, or in the process of, meiosis or which are mature gametes will lead to gametes which are able to participate in fertilization but which lead to early or late death of the developing zygote.
>
> (3) Reciprocal translocations and inversions present in gametes of irradiated individuals may permit normal development of the offspring but a fraction — as high as fifty percent — of the gametes produced by their heterozygotes with chromosomal aberrations will cause death of zygotes among their potential children.[86]

From these he concludes that a given dose of radiation exposure will produce fewer transmissible chromosomal aberrations than point mutations.[87] There is insufficient data upon which a doubling dose for the defects due to gross chromosome aberration can be estimated.[88] It must be further noted that there is still a question regarding whether the chromosomal aberration associated with Mongolism, which is due to a phenomenon known as chromosomal nondisjunction, occurs before or after fertilization of the egg.[89] This question is also still open with regard to Turner's and Klinefelter's syndromes which are associated with nondisjunction of the sex-chromosomes.[90]

II. LEGAL CONCEPTS

A. Limitations of this Discussion

In discussing the legal significance of exposure the term "genetic injuries" will be used to refer to genetic changes, gene mutations, and chromosomal aberrations which are induced by one mutagenic agent only, namely ionizing radiation. It must

85. *Id.* at 96.
86. STERN 513.
87. *Id.* at 514.
88. U.N. SCIENTIFIC COMMITTEE 101.
89. MUTATIONS 231-32.
90. *Ibid.* Note that there is marked maternal age-dependence in Mongolism and that it has also been noted in Klinefelter's syndrome but not in Turner's syndrome.

also be remembered that genetic changes or mutations in the germ cells (the reproductive cells) do not cause any apparent damage or injury to the person in whom the mutation takes place. Their effects are manifest only in the immediate offspring or remote descendants of the individual in whom the mutation occurs. Ionizing radiation sufficient to produce germ cell mutations may be sufficient to produce acute or latent somatic effects including somatic mutations and these might be injurious to the exposed individual. Our concern, however, is only with the effect on the genes of the germ cells and possible liability for injuries to the individuals who are irradiated, or their offspring. The problems involved in resolving all of these damage issues in ordinary personal injury trials will also be discussed and a different method for handling such cases will be suggested.

It is quite clear that radiation as well as many chemical and pharmacological agents, certain maternal diseases, certain fetal environmental conditions, and maternal trauma are capable of producing effects on the developing human embryo or fetus from the time of conception until parturition (birth). Such agents are known as teratogens. It is also known that certain agents are more effective during particular periods of the pregnancy.[91] These effects can result in embryonic or fetal death and can terminate the pregnancy in a miscarriage or a stillbirth. They can also result in children with congenital abnormalities which range from severe defects to very mild impairments. These fetal or embryonic effects which occur between conception (the formation of the zygote by fertilization of the egg by the sperm) and birth are not the subject of this discussion. Rather it will cover only preconception injuries to children produced by germ-cell gene mutation. However, in the case of a child actually born with a congenital defect, induced embryonic or fetal changes from known or unknown agents affecting it during gestation must be considered in determining the probability that a preconception radiation-induced mutation produced the particular abnormal condition.

B. Liability for Preconception Injuries

Any discussion of the legal interests of children born with

91. Witness the recent publicity associated with thalidomide and periodic attention given to German measles (rubella) during the first trimester of pregnancy. See N.Y. Times, Nov. 15, 1962, p. 35, col. 8; Ann Arbor News, Nov. 15, 1962, p. 29, col. 1-5.

radiation induced hereditary abnormalities and the rights of the parents of such children should start with a consideration of liability for preconception injuries generally,[92] with particular emphasis being placed on the rationale for allowing and disallowing recovery and the possible limitations found in current cases which permit recovery.

1. *Liability for Prenatal Injuries in General*

The issue in all cases involving prenatal injuries is whether the child at the time of injurious impact, *i.e.*, prior to its birth, has a legal personality which the law will protect.[93] From 1884 until 1946 the American courts consistently answered this question in the negative.[94] The existence of a cause of action for prenatal injuries was denied on one or both of the following grounds:

(1) The unborn child had no juridical existence separate from its mother and therefore there was no person to whom a defendant could owe a duty.[95]

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92. For a discussion of what rights are the parents' and what rights are the child's, see PROSSER, TORTS 698-705 (2d ed. 1955); Annot., 32 A.L.R.2d 1060 (1953); Annot., 37 A.L.R. 11 (1925).

A number of courts have concluded that there may be recovery for medical expenses incurred, without reference to the old doctrine of loss of services at all. PROSSER, TORTS 700 (especially footnote 25) (2d ed. 1955).

A parent may not recover where the defendant owes the child no duty of care. See PROSSER, TORTS 701 (especially footnote 37) (2d ed. 1955).

93. White, *The Right of Recovery for Prenatal Injuries*, 12 LA. L. REV. 383 (1952).

94. See STASON, ESTEP & PIERCE, ATOMS AND THE LAW 202-07 (1959). See also 2 HARPER & JAMES, TORTS 1028-31 (1956); PROSSER, TORTS 174-75 (2d ed. 1955); Annot., 10 A.L.R.2d 639 (1950); Annot., 10 A.L.R.2d 1059-72 (1950). See also White, *The Right of Recovery for Prenatal Injuries*, 12 LA. L. REV. 383 (1952).

It must be noted that recovery was allowed in Quebec Province in Canada in 1933 in the case of Montreal Tramways v. Levielle, 4 D.L.R. 337 (1933) (involving alleged prenatal injuries producing a clubfoot in a surviving child). The court held:

> "The wrongful act which constitutes the crime may constitute also a tort, and if the law recognizes the separate existence of the unborn child sufficiently to punish the crime, it is difficult to see why it should not also recognize its separate existence for the purpose of redressing the tort.
>
> "If a right of action be denied to the child, it will be compelled, without any fault on its part, to go through life carrying the seal of another's fault and bearing a very heavy burden of infirmity and inconvenience without any compensation therefor."

Id. at 344.

95. See generally, White, *The Right of Recovery for Prenatal Injuries*, 12 LA. L. REV. 383 (1952); Annot., 10 A.L.R.2d 1059 (1950). See also Dietrich v. Northampton, 138 Mass. 14, 52 Am. Rep. 242 (1884). It should be noted that the *Dietrich* case was followed in Massachusetts until 1960 when in Keyes v.

(2) The difficulty of proving any causal connection between the force put in motion by the defendant and the claimed injury was too great, thereby creating the spectre of a flood of fictitious and fraudulent claims.[96]

The denial of the existence of a cause of action was the subject of general criticism by most legal scholars and writers but courts uniformly denied recovery.[97]

In 1946 the trend toward allowing recovery for prenatal injuries began.[98] This trend now has advanced to the point where recovery for all injuries received after the moment of conception is granted in most jurisdictions in which the question has been litigated, at least in the case of a child who is born alive.[99] The following reasons have been given for permitting recovery:

(1) Biologically, from the moment of conception onward,

Construction Service Inc., 340 Mass. 633, 165 N.E.2d 912 (1960) separate existence of a viable unborn child for purposes of tort liability was recognized.

96. PROSSER, TORTS 698-705 (2d ed. 1955); Annot., 10 A.L.R.2d 1059 (1950); White, *The Right of Recovery for Prenatal Injuries*, 12 LA. L. REV. 383 (1952); McBride and Norvell, *The Extension of Tort Liability in the Field of Prenatal Injuries*, 26 INS. COUNSEL J. 148 (1959). See also concurring opinion of Justice Duckworth in Hornbuckle v. Plantation Pipeline Co., 212 Ga. 504, 93 S.E.2d 727, 729 (1956).

97. PROSSER, TORTS 698-705 (2d ed. 1955); 2 HARPER & JAMES, TORTS 1028-31 (1956); White, *The Right of Recovery for Prenatal Injuries*, 12 LA. L. REV. 383 (1952); STASON, ESTEP & PIERCE, ATOMS AND THE LAW 207 n. 324 (1959); Annot., 10 A.L.R.2d 639, 1059 (1950).

98. Bonbrest v. Katz, 65 F. Supp. 138 (D.D.C. 1946) (regarded a viable fetus as having a legal existence for purposes of tort liability).

99. See STASON, ESTEP & PIERCE, ATOMS AND THE LAW 207-211 (1959) (especially cases cited). It should be noted that New York in Woods v. Lancet, 303 N.Y. 349, 102 N.E.2d 691 (1951) began allowing recovery for prenatal injuries and in Kelly v. Gregory, 282 App. Div. 542, 125 N.Y.S.2d 696 (1953), noted 29 N.Y.U.L. REV. 1154 (1954), extended allowable recovery to all post-conception injuries. Illinois in Amann v. Faidy, 415 Ill. 422, 114 N.E.2d 412 (1953) abandoned the doctrine of Allaire v. St. Luke's Hospital, 184 Ill. 359, 56 N.E. 638 (1900) and began allowing recovery. The viability test was abandoned in Daley v. Meier, 178 N.E.2d 691 (Ill. App. 1961) and Sana v. Brown, 183 N.E.2d 187 (Ill. App. 1962). So did New Jersey in Smith, v. Brennan, 31 N.J. 353, 157 A.2d 493 (1960) reversed Stemmer v. Kline, 128 N.J.L. 455, 26 A.2d 489 (1942), and began allowing recovery, extending it to conception. Georgia abandoned the viability requirement in 1956, allowing recovery for any proved tortious injury occurring after conception. Hornbuckle v. Plantation Pipe Line Co., 212 Ga. 504, 93 S.E.2d 727 (1956). Pennsylvania also began allowing causes of action from the point of conception in Sinkler v. Kneale, 401 Pa. 267, 164 A.2d 93 (1960). The Pennsylvania case involved a Mongoloid child allegedly produced by an automobile collision during the first month of its mother's pregnancy. New Hampshire also no longer requires viability, Bennet v. Hymers, 101 N.H. 483, 147 A.2d 108 (1958). In Michigan for all purposes of construction a child *en ventre sa mere* is considered a child *in esse*, if it will be for the child's benefit to be so considered, LaBlue v. Specker, 358 Mich. 558, 100 N.W.2d 445 (1959).

the child has an independent existence, depending on the mother only for sustenance and protection.[100]

(2) Problems of difficulty of proof or finding a causal relationship (a) are beside the point in determining the sufficiency of a cause of action, (b) are not special to this particular kind of suit but are common in the negligence and workmen's compensation cases which are regularly decided, and (c) can be adequately solved by the court if it will accept its responsibility for determining the sufficiency of evidence before submitting cases to the jury and the weight and sufficiency of the evidence before allowing jury verdicts to stand.[101]

(3) The law recognizes the existence of the unborn child sufficiently to protect its property, its rights of inheritance, and to extend to it the protection of the criminal law and therefore should recognize its separate existence for the purpose of redressing torts.[102]

Although recovery was initially limited to cases of injury occurring after the unborn child was viable, *i.e.*, capable of life

100. At conception the zygote which develops into the child acquires 23 pairs of chromosomes, with one of each pair coming from the father and one from the mother. It is a distinct biological entity with a different chromosomal and genetic make-up from the mother. See STERN 36-38, 7-35. See also, ROBERTS, AN INTRODUCTION TO MEDICAL GENETICS 3 (2d ed. 1959).

The mother's biological contribution from conception on is nourishment and protection, but the fetus, embryo, or zygote is a separate organism and remains so throughout its life. Kelly v. Gregory, 282 App. Div. 542, 125 N.Y.S.2d 696 (Sup. Ct. App. Div. 3d Dept. 1953).

"While it is a fact that there is a close dependence by the unborn child on the organism of the mother, it is not disputed today that the mother and child are two separate and distinct entities, that the unborn child has its own system of circulation of the blood separate and apart from the mother; . . . that there is no dependence by the child on the mother except for sustenance." Justice Brogan's dissent in Stemmer v. Kline, 128 N.J.L. at 466, 26 A.2d at 687 (1942).

101. PROSSER, TORTS 698-705 (2d ed. 1955); Annot., 10 A.L.R.2d 1059 (1950); White, *The Right of Recovery for Prenatal Injuries*, 12 LA. L. REV. 383 (1952).

"But such difficulty of proof or finding is not special to this particular kind of lawsuit (and it is beside the point, anyhow in determining sufficiency of a pleading). Every day in all our trial courts (and before administrative tribunals such as workmen's compensation boards) such issues are disposed of, and it is an inadvisable concept that uncertainty of proof can ever destroy a legal right." Woods v. Lancet, 303 N.Y. 349, 346, 102 N.E.2d 691, 695 (1951). See also Williams v. Marion Rapid Transit Inc., 152 Ohio St. 114, 87 N.E.2d 334 (1949) for the proposition that law should keep pace with science in dealing with the question of difficulties of proof.

102. PROSSER, TORTS 698-705 (2d ed. 1955); Annot., 10 A.L.R.2d 1059 (1950); White, *The Right of Recovery for Prenatal Injuries*, 12 LA. L. REV. 383 (1952). See 57 AM. JUR. *Wills* § 154 (1948); 16 AM. JUR. *Descent and Distribution* § 80 (1938); 26 AM. JUR. *Homicide* § 32 (1940); 1 C.J.S. *Abortion* §§ 1-3 (1936) and cases cited therein.

outside of the uterus, it is now generally being allowed for all postconception injuries on the grounds that (a) a limitation based on viability is arbitrary and artificial, (b) viability is difficult to ascertain in many cases, (c) many serious prenatal injuries are more likely to be inflicted during the first trimester of pregnancy and therefore before viability, and (d) from the time of conception onward the fetus becomes a distinct biological organism.[103]

None of these cases, however, dealt with preconception injuries, as such. One case, *Morgan v. United States*, did raise the issue of liability for a preconception "impact,"[104] but it was dismissed on the grounds of a two-year statute of limitations and on the now reversed Pennsylvania doctrine disallowing all claims for prenatal injuries. The *Morgan* case involved, among other things, the claim of a mother as personal representative of a child who suffered from birth defects allegedly the result of improper blood transfusions given about two years before conception.[105] Injuries in the case of improper blood transfusions producing Rh or other blood group antibodies in the mother, however, unlike genetic injuries, involve postconception injuries resulting from the effects of a preconception act, the injury in fact occurring after the maternal antibodies have been transferred to the developing fetus where they affect the fetal blood.[106] Nevertheless, the antibodies are formed shortly after the time of the transfusion which is usually before conception — and was before conception in the *Morgan* case.[107] Consequently the case presented a situation analogous to the genetic injury cases where both impact and injury occur before conception.

No courts or legal writers in discussing prenatal injuries have satisfactorily resolved the question of liability before con-

103. White, *The Right of Recovery for Prenatal Injuries*, 12 LA. L. REV. 383 (1952). It should be noted that with regard to fetal injuries, the first trimester of pregnancy, the period of organogenesis, is the most sensitive period for fetal injuries due to such agencies as radiation or German measles (rubella). See Bennett v. Hymers, 101 N.H. 483, 147 A.2d 108 (1958). See Sinkler v. Kneale, 401 Pa. 267, 164 A.2d 93 (1960) for the proposition that since the fetus is regarded as having an existence as a separate creature from the moment of conception, viability is irrelevant. See Smith v. Brennan, 31 N.J. 353, 157 A.2d 493 (1960) for the proposition that the viability rule is impossible of practical application.

104. 143 F. Supp. 580 (D.N.J. 1956). Pennsylvania initially denied recovery; Berlin v. J. C. Penney Co., 339 Pa. 547, 16 A.2d 28 (1940). The *Berlin* case was reversed in the *Sinkler* case.

105. Morgan v. United States, 143 F. Supp. 580 (D.N.J. 1956).

106. WINTROBE, CLINICAL HEMATOLOGY 756-64 (5th ed. 1961).

107. *Ibid.*

ception and the separate biological existence of the child. Even the *NACCA Journal*, in discussing the first abandonment of the viability test by a state court of last resort, acclaimed the decision because the court in simple, uncluttered language decided that the legal personality began from the instant of conception.[108] It stated that the protection accorded to human life by the common law ordains that it be secured at the beginning as an acorn is the forerunner of the oak and the seed the antecedent of the garden.[109] Obviously *conception has occurred* in both the acorn and the seed.[110]

Only in one other case, *Hornbuckle v. Plantation Pipe Line Co.*, is mention made of preconception injuries. In a concurring opinion, disagreeing with allowing recovery for prenatal injuries to a nonviable fetus, it was pointed out that the extension of recovery back to the time of conception opened up the twin problems of difficulty of proof and fictitious fraudulent claims to the same extent to be found in permitting recovery for preconception injuries perhaps several generations removed.[111]

2. Extension to Preconception Injuries

The issue then is whether the reasons for the rule allowing recovery for prenatal injuries received after conception will justify recovery for preconception injuries caused by radiation-induced germ-cell gene mutations. The law of property and descent and distribution does not extend its protection to children prior to conception. This is also true of the criminal law.[112] Furthermore, there is no independent biological organism before

108. See Lambert, *Comment on Leading Decisions*, 19 NACCA L.J. 230 (1957). The decision of the Supreme Court of Georgia in Hornbuckle v. Plantation Pipe Line Co., 212 Ga. 504, 93 S.E.2d 727 (1956) was the subject of the discussion. The commentator concluded that the law is on the side of medical science in the edifying ruling that legal existence commences at conception and not at some speculative indeterminate later point in fetal life.

109. Lambert, *Comment on Leading Decisions*, 19 NACCA L.J. 230, 239 (1957).

110. The acorn and the garden seed in common usage are both fertilized and are capable of growing into a mature tree or plant. Pollination has already occurred. Therefore, conception has occurred.

111. 212 Ga. 504, 506, 93 S.E.2d 727, 729 (1956).

"If a baby can sue for injuries sustained five seconds after conception, as the majority rules, why not allow such suits for injuries before conception, even unto the third and fourth generations?" (Concurring opinion of Chief Justice Duckworth).

112. Thus, with regard to the male, castration which will quite effectively do away with all of the future potential offspring of a given individual is not treated by the criminal law as homicide of the unborn children, who might have resulted from the use of the procreative powers which were destroyed by the act of castration.

conception. The germ cells of the father and mother are chromosomally and immunologically identical to the other cells of the mother or father, except that the matured gametes of each will have the haploid rather than the diploid number of chromosomes. Only after conception, when the zygote has formed from the union of the egg and sperm, does a biologically distinct organism with a different chromosomal, genetic, and immunological make-up from the mother or father come into being. In humans, the normal future of the unfertilized egg or the sperm is *not* development into a distinct organism, unless fertilization and thus conception occur.

The absence of these reasons for permitting recovery for postconception prenatal injuries, however, should not lead to denial of recovery for genetic injury. If the proof-of-causal-connection obstacle can be surmounted and administrative difficulties can be met the law cannot afford to deny recovery for preconception injuries if a child is born and lives with a handicap created by defendant's radiation source under such circumstances that he would be liable if conception had already taken place.[113] The first question therefore is whether or not proof of causal connection is possible.

In dealing with alleged negligently inflicted mental disturbances which present a similar problem of difficulty of proof, many courts now hold that such claims should not be denied arbitrarily if they are capable of clear medical proof.[114] These courts take the position that difficulty of proof in individual situations should not be the basis for barring all actions, but rather that the quality and genuineness of proof in each individual case should be weighed and reliance placed on the wise use of expert medical testimony and the ability of the court and jury to weed out dishonest claims.[115] Under this approach it is essential to understand the scientific facts as to which, if any, radiation-induced preconception mutations are capable of clear medical proof.

In considering the available medical proof two different types of recovery must be considered. One is for increased risk of *future* defective offspring. The other is recovery for specific diseases or defects manifested in an *existing* offspring of exposed ancestors.

113. See Note, 29 N.Y.U.L. REV. 1154 (1954).
114. Ferrara v. Galluchio, 5 N.Y.2d 16, 152 N.E.2d 249 (1958).
115. Batalla v. State of New York, 10 N.Y.2d 237, 176 N.E.2d 729 (1961).

a. Recovery for Increased Risk of Future Manifestations of Genetic Damage. — Under existing rules governing proof of causal connection it is clear that no recovery can be had by persons exposed to radiation for the increased probability of bearing a defective child. This is well illustrated by the following summary of scientific evidence made by Dr. Stern:

> "It has been estimated that from 4 to 6 per cent of all children either possess or will develop tangible defects, sometimes slight, sometimes severe, of a skeletal, neuromuscular, sensory, physiological, or other nature. In from 1 to 2 per cent of all births, the defects are clearly discernible at birth. If one regards half of all defects, or from 2 to 3 per cent, as being genetically caused, this is probably an underestimate. If the germ cells of parents have been exposed to artificial radiation, how many additional defective children will be born as a result of mutations induced in these germ cells? This question may be asked from the 'private' point of view of individual parents, who want to know how much increased is the probability of their producing a defective child, or from the 'public' point of view of the population who wants to know the additional number of defectives to be expected."[116]

Based on a series of assumptions Stern concludes that between 1.95 and 5.9 or an average of 4 percent of all parental germ cell mutations will be expressed in some manner in the first generation after they have occurred.[117]

He then goes on to state:

> "Since the frequency of induced and expressed mutants

116. See STERN 514-15.

117. *Id.* at 515-17 (especially note table at 515).

"As bases of very provisional answers to these questions, we use the following, earlier-derived estimates: (1) number of mutable genic loci = 10,000; (2) number of induced mutations per locus per roentgen = 2.5×10^{-7} for acute and 0.625×10^{-7} for chronic exposures. An additional requirement for answering these questions is an estimate of the proportion of dominant to recessive mutations in man. This is a ratio whose value is not known. There are rather few dominant, defect-causing genes with complete penetrance, and probably more recessive, defect-causing genes with simple inheritance. Between these extremes, however, lies the whole range of conditionally dominant mutants with incomplete and often very low penetrance, and all those recessive mutants which in heterozygotes produce phenotypic traits detectable in some way even if the heterozygous carriers are normal." *Id.* at 515. See also *id.* at 497-98. The assumption that chronic exposures are one-fourth as effective as acute exposures in producing mutations is based on the mouse experiments of Russell and Russell discussed at 71 and 72 *supra*, and accompanying text.

depends on the exposure received, we shall assume a specific dose, 10 r, given *to both* parents of a pair or to *all prospective parents of a population.* For lower or higher doses the expectations for expressed mutants are proportionally lower or higher. We have estimated earlier that an acute dose of 10 r will induce a mutation in approximately 2.5 out of 100 gametes (postulating that the same figure is valid for eggs and sperm). Since perhaps 4 per cent [1.45-5.9 percent] of all induced mutants are expressed in the offspring of a single exposed parent, the probability of affected offspring from both exposed parents is 2.0 x 0.025 x 0.04 or 0.002 or 2 in 1,000 [.2 of 1 percent]. This is a low probability, particularly in comparison with the general probability of affected offspring from nonexposed parents, which was earlier estimated as lying between 4 per cent and 6 per cent. . . . *An individual parental pair, acutely exposed to 10 r beyond background radiation has thus a probability of from 95.8 to 93.8 per cent of having a normal child as compared to the probability of from 96 to 94 per cent from unexposed parents* [a difference of .2 of 1 percent]. . . . If the parents have been exposed chronically at low intensities, all figures given for high-intensity radiation can be reduced to at least one-fourth of those for acute exposure."[118] (Emphasis added.)

If *only one rather than both parents* is exposed to 10 r of acute radiation the probability of having a normal child is only .1 of 1 percent less than in the case of unexposed parents, since the mutation rate increase would occur in only one parent, and for all practical purposes would be no different from the unexposed cases.

Based on the above reasoning and assumptions (all of which assumptions are made to err on the side of safety and not to underestimate the harmful mutagenic effect of ionizing radiation), it has been stated that if a given individual receives a preconception gonadal (germ cell) dose of radiation short of that which approximates the mid-lethal dose in humans, it is most highly improbable that the individual will have a defective first generation child whose defects could be attributable to that dose.[119]

118. STERN 517.

119. Personal communication from Dr. James F. Crow. All assumptions are based on the propositions that (1) radiation has a linear mutagenic effect down to zero dose, with increase in mutation rate linearly proportional to dose, and (2)

Stern, in referring to irradiation of *both* parents, further states:

> "Even with 50 r — a considerably higher acute exposure than that assumed in the foregoing discussion — the calculated induced frequency of affected children would only be 0.01, which is one-fourth or one-sixth of the spontaneous rates 0.04 and 0.06. Unless prospective parents are exposed to acute doses much larger than 50 r, the probability of their having normal children remains very great. If the parents have been exposed chronically at low intensities, all figures given for high-intensity radiation can be reduced to at least one-fourth of those for acute exposure."[120]

The 94.1 to 98.05 percent of the mutants (those other than fully penetrant dominants) which were discussed above in Stern's illustration would not appear phenotypically in the first generation offspring, but would appear, if at all, only in subsequent generations.[121] Their probability of phenotypic expression would be no greater in any subsequent generation than it was in the first, because the factors governing expression would be substantially the same from one generation to the next. Consequently, the reasons for not allowing recovery in the usual personal injury context for mutants expressed in the first generation are just as compelling for disallowing recovery for mutants in any particular subsequent generation.[122]

These figures make it perfectly clear that the probability of any exposed person actually having a deformed offspring is much less than 50 percent. Therefore, *under existing rules concerning proof of causation, no recoveries should be permitted for possible future manifestations of genetic damage.*[123]

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that all mutations produced by radiation are harmful. See RESEARCH COUNCIL (1956) 3-30. For further support of this proposition see Stevenson, *The Genetic Hazards of Radiation*, 181 PRACTITIONER 559-71 (1958).

120. STERN 517.

121. The mutants which would not appear phenotypically in the first generation are based on Stern's conclusions in note 117 *supra* and accompanying text. They are not to be confused with the probability (expressed as a per cent chance) of having a normal child after both parents have been acutely exposed to 10 roentgens, referred to in Stern's example quoted in the text accompanying note 118 *supra*.

122. "What are the prospects for the grandchildren and later descendants of irradiated parents? In general, they are not much different from those of the first generation. Genes with dominant effects of low penetrance have unchanged chances of expressing themselves in future generations, and the same is true for recessives becoming homozygous." STERN 517.

123. See STASON, ESTEP & PIERCE, ATOMS AND THE LAW 428 (1959) for the

b. Recovery for Specific Genetic Defects or Diseases after Manifestation. — At the outset, injuries resulting from radiation induced preconception genetic mutations present a more difficult problem than postconception radiation injuries because the injury must be established not only (1) to be of a hereditary nature rather than a defect or disease which resulted from effects of known or unknown agents operating on the fetus after conception but also (2) to be the result of a harmful mutation induced by the exposure of the parent or ancestor to defendant's radiation source rather than of a spontaneous mutation in either parent, or of a mutation induced in the other parent by an exposure to some other known or unknown mutagenic agent or of a recessive sex-linked or autosomal allele or dominant allele with reduced penetrance or variable expressivity transmitted through "normal" carriers to the child in question. Furthermore, preconception genetic injuries do not necessarily manifest themselves at birth or in early infancy, but can appear after puberty is reached, *e.g.*, schizophrenia.

The difficulty of determining whether or not the particular defect or disease is hereditary is illustrated by the category II defects. These were noted in earlier discussion to be "developmental defects," in which the role of hereditary versus fetal environment is not known.[124] They are observable in 1.5 percent of live births and by age five years an additional 1 percent of living children will be observably affected.[125] If stillbirths were also included the percent of affected children would be even higher.[126] Consequently more than two percent of the population under five years of age are affected by a number of diseases and defects in which heredity may or may not play a role. Another possible illustration is that group of cases involving chromosomal nondisjunction in which it is still not clear whether the nondisjunction occurs before, during, or after fertilization (conception).[127]

existing rules governing proof of causation: the more-probable-than-not test. Professor Leon Green suggests that if enough evidence is adduced to support a reasonable inference that defendant's conduct played a part in the result, a case which is submissible to the jury has been made. This, however, is not the existing rule. Furthermore, the probability of future manifestations of genetic damage would be so small that recovery most likely would be denied under any reasonable interpretation of Professor Green's proposed rule. See Green, *The Causal Relation Issue In Negligence Law*, 60 MICH. L. REV. 543, 561 (1962).

124. U.N. SCIENTIFIC COMMITTEE 87. See also note 45 *supra* and accompanying text.

125. *Ibid.*

126. *Ibid.*

127. See notes 89 and 90 *supra* and accompanying text.

On the other hand, enough is known about the genetic mechanisms of certain diseases or defects maintained by point mutations to permit recovery in some radiation cases if the existing rule for proof of causal connection is used, *i.e.*, more probable than not.[128] However, since planned breeding and genetic analysis cannot be employed in humans, there are difficulties in relating even these defects to specific mutant alleles.[129] Because of these difficulties only certain defects have been carefully investigated to date.[130] Therefore, one caution must be kept in mind in considering the following discussion: the specific defects discussed below do not include all abnormal traits whose mutation rate is determined by point mutation but only those about which at present we know the most. Another limitation of our present scientific knowledge is that not all cases of the particular abnormalities here listed are invariably the result of the particular kind of mutation which usually is responsible for such a defect.[131]

(1) Dominant Mutations.

The diseases appearing in children known as epiloia, achondroplasia, aniridia, microphthalmos, retinoblastoma, neurofibromatosis, arachnodactyly, and acrocephalosyndactyly have been reasonably well established to be transmitted usually by autosomal *dominant* and fully penetrant alleles whose frequencies are maintained by point mutation.[132] Since these defects are

128. See STASON, ESTEP & PIERCE, ATOMS AND THE LAW 428 (1959).

129. Some of these difficulties are specific to dominant, some to sex-linked, some to recessive gene mutations, and some are common to all three. The following are common to all three:

(1) Certain mutant gene traits are mimicked by phenocopies.
(2) Certain traits which are difficult if not impossible to distinguish clinically are sometimes determined by mutations on different chromosomes.
(3) Some clinically identical traits seem to be inherited as if they were autosomal dominant at some times and recessive at other times.
(4) Some traits, though apparently inherited in the same manner show differences between families which suggest that the causal mutations are different in kind.

U.N. SCIENTIFIC COMMITTEE 89-90.

130. *Id.* at 90. See also STEVENSON, COMPARISON OF MUTATION RATES AT SINGLE LOCI IN MAN, EFFECT OF RADIATION ON HUMAN HEREDITY 125-37 (1957) [hereinafter cited as STEVENSON].

131. U.N. SCIENTIFIC COMMITTEE 90. See also STEVENSON 130-137.

132. See U.N. SCIENTIFIC COMMITTEE 103, Table IV. Epiloia is a disease consisting of mental deficiency, sebaceous (oil gland) tumors of the skin, epileptic fits, fibrosis of the brain, and kidney tumors. TABER, CYCLOPEDIC MEDICAL DICTIONARY E-40 (7th ed. 1957). Achondroplasia is a form of dwarfism characterized by a deficit in the formation of cartilage at the growth centers of long bones. *Id.* at A-13. Aniridia is a disease characterized by congenital complete or partial

perpetuated by point mutation it is valid for purposes of proving legal causation to assume that 50 and 200 rads constitute a doubling dose for acute and chronic exposures respectively.[133]

If a child definitely diagnosed as being affected with any of these defects were to be born to a parent who had received an acute dose in excess of 100 rads (twice the doubling dose) or a long term dose in excess of 400 rads (twice the doubling dose) and sufficient pedigree data were available to substantiate the autosomal dominant transmission in the affected individual, then it could be established, using a more-probable-than-not test of causation, that the exposure in question was legally responsible for the defective child. The exposure would have more than tripled the incidence of harmful point mutations in the exposed parent and thereby more than doubled the normal incidence of this disease or defect, considering the potential contribution of each parent.[134] Since these diseases are transmitted by dominant inheritance there would be no problem of transmitting these defects to subsequent generations by not-observably-affected children of the irradiated parent.

The occurrence of these diseases, however, is so extremely rare that even if the number of cases were doubled, for practical purposes, litigation involving offspring of exposed parents calling for legal solutions would arise only once in a good many years.[135] This number of cases certainly would not warrant crea-

absence of the iris of the eye. *Id.* at A-59. Microphthalmos is a condition characterized by abnormally small eyes. *Id.* at M-37. Neurofibromatosis is a condition in which there are tumors of various sizes on the peripheral nerves. *Id.* at N-19. Arochnodactyly is a condition in which fingers and sometimes toes are abnormally long, slender, and curved. It can be accompanied by other pathological conditions and then is called Marfan's syndrome. *Id.* at A-78. Acrocephalosyndactyly is a condition characterized by a malformed skull having a high or peaked appearance due to premature closure of the coronal, sagittal, and lambdoidal sutures. It can be accompanied by brain damage. *Id.* at A-20. A retinoblastoma is a malignant tumor of the nerve cells of the retina of the eye.

133. See notes 79-80 *supra* and accompanying text.

134. The incidence of harmful point mutations would be tripled rather than quadrupled by an exposure to two times the doubling dose of radiation because a doubling dose is that dose which causes an increased incidence of abnormal mutations equal to those already in existence in the population as a result of spontaneous mutation. An additional doubling dose would also cause an additional number of mutations equal to those in the population resulting only from spontaneous mutation. Consequently, a person receiving two times the doubling dose would have a probability of carrying harmful mutations equal to three times that of an unexposed individual.

135. The combined total frequency of all of the above mentioned autosomal dominant diseases (computed on a world-wide basis) is about 3 per 100,000 births, or .003 percent, contrasted with a frequency of about 4 percent for all diseases or defects with a genetic component. If adjusted for presumptive phenocopies, the figures would probably be even lower than .003 percent. The number

tion of new legal concepts for their solution. Furthermore, if either of the parents had been exposed to large amounts of medical or dental X-ray or other potentially mutagenic agents prior to conception of the affected child then even a higher dose would be required to fulfill the more-probable-than-not test. Actually this type of genetic damage would represent only a minute fraction of the potential harmful genetic impact of the exposures in question.[136]

(2) Autosomal Recessive Mutations.

Certain other diseases or defects such as juvenile amaurotic idiocy, albinism, ichthyosis congenita, total color blindness, infantile amaurotic idiocy, amyotonia congenita, epidermolysis bullosa, microcephaly, and phenylketonuria have been determined to be transmitted usually by autosomal *recessive* (as contrasted with dominant in the previous discussion) alleles whose

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of people occupationally or accidentally exposed to more than 100 rads acutely or 400 rads chronically since the beginning of the Manhattan Project is very small. Consequently, the probability of a person receiving 100 rads acute or 400 rads chronic exposure and producing a child with one of the above discussed defects is infinitesimally small. See U.N. SCIENTIFIC COMMITTEE 103 (incidence of the diseases), 140-144 (analysis of past accidents on a world-wide basis). See also *Hearings on Employee Radiation Hazards and Workmen's Compensation Before the Subcommittee on Research and Development of the Joint Committee on Atomic Energy*, 86th Cong., 1st Sess., at 855-58 (1959) (summary of licensee radiation incidents). See also *Selected Materials on Employee Radiation Hazards and Workmen's Compensation, Joint Committee on Atomic Energy*, 86th Cong., 1st Sess., at 254-327 (1959) (summary of accidents and incidents involving radiation in atomic energy activities). By the fall of 1958 a total of about 60 persons had received exposures in excess of prescribed limits for a short term period but less than 3 rem in a week. Through the same period 28 persons employed by licensees received estimated exposures in excess of 3 rem per week. *Id.* at 97.

A world-wide analysis which contains all reported large exposures from 1945 through early 1962 shows 7 men acutely exposed to more than 50 rads, five of whom were exposed to over 200 rads acutely, at the Y-12 plant in Oak Ridge in 1958. It also shows 9 technicians who could have conceivably received more than 50 rads of gonadal exposure to pulsed X-rays at a Lockport, New York, radar installation, 2 Russians (survival not indicated) who received 300-450 r of total body neutron and gamma exposure from a reactor, 4 workers at the Argonne laboratory who received doses from 10.8-159 rads of total body exposure, 3 fatal exposures to critical masses or excursions at Los Alamos, 5 cases of exposure of less than 100 rem of soft exposure and 10 rad penetrating exposure from Los Alamos, 1 asymptomatic case from Los Alamos with the dose not calculated, 1 case with 400 r of soft and 40 r of penetrating exposure from Los Alamos, and 6 Yugoslavians with acute exposures in excess of 200 rads (reactor incident — 1 death and 5 survivors). Altogether there have been about 28-32 survivors of nuclear radiation accidents throughout the world since 1945 who have received potential acute exposures in excess of 50 rads to their reproductive organs. The number receiving more than 100 rads probably is no more than 20. See also notes 139 and 146 *infra*.

136. Most mutations are recessive and most have a very small direct effect on any one generation. See notes 64 and 70 *supra* and accompanying text.

frequencies are maintained by point mutation.[137] Consequently, the 50 and 200 rad doubling dose figures are again valid.[138] These diseases will not be expressed unless both the exposed and unexposed parents contribute an abnormal allele. Consequently, given a definitively diagnosed child with sufficient pedigree to establish recessive autosomal transmission, a more-probable-than-not test of causation could be met in cases in which the exposed parent received more than the acute or long-term doubling dose, rather than a tripling dose as in the case of dominant mutations. This conclusion, however, is subject to the same qualifications as in the case of the dominant defects regarding other preconception exposures to mutagenic agents.

Because these diseases are transmitted by recessive alleles they may be passed on by healthy observably unaffected carriers through many generations. Consequently, the pedigree of the exposed parent would have to be examined in considerable detail to determine the probability of the abnormal allele's origin in an affected ancestor of the exposed parent. This probability must be considered in determining the contributory effect of the radiation exposure in question. In the case of these recessive defects and diseases the question would be whether or not the radiation exposure of the parent was a substantial contributing factor in the production of the defective child.[139] In any event, again the occurrence of these particular recessively inherited diseases is so extremely rare that even if the number of cases

137. See U.N. SCIENTIFIC COMMITTEE 104, Table VI.

Juvenile amaurotic idiocy is a mental deficiency seen in small children in which there is increasing failure of vision and eventual death. TABER, CYCLOPEDIC MEDICAL DICTIONARY I-2 (7th ed. 1957). Albinism is a condition characterized by abnormal total or partial absence of pigment in the skin, hair, and eyes which is frequently accompanied by visual difficulties. *Id.* at A-33. Ichthyosis congenita is a congenital abnormality of the skin characterized by dryness, harshness, and scaliness. *Id.* at I-1. Total color blindness is a condition characterized by total inability to identify colors. *Id.* at C-74. Infantile amaurotic idiocy is a mental deficiency seen in infants in which there is increasing failure of vision and eventual death. *Id.* at I-2. *Amyotonia congenita* is a congenital disease characterized by tonic muscle spasm and rigidity of certain muscles when an attempt is made to move them after a period of rest or when mechanically stimulated. The spasm tends to disappear after use of the muscles. *Id.* at A-47. Epidermolysis bullosa is a disease characterized by large skin blisters. *Id.* at E-38. Microcephaly is a condition characterized by an abnormally small head accompanied by marked mental deficiency. *Id.* at M-35. *Phenylketonuria* is a disease of infants characterized by mental deficiency, behavioral disorders, central nervous system damage, and tendency toward convulsive disorders, associated with excretion of phenylpyruvic acid in the urine and caused by an inability to metabolize an amino acid, phenylalanine, to tyrosine with the consequent build-up of phenylalanine. NELSON, TEXTBOOK OF PEDIATRICS 259-260 (7th ed. 1959).

138. See notes 79-80 *supra* and accompanying text.

139. PROSSER, TORTS 218-22 (2d ed. 1955).

were doubled, legal cases involving children of sufficiently exposed parents would arise only once in many years.[140] Again, these particular diseases and defects would represent only a minute fraction of the potential harmful genetic impact of the exposures in question.[141]

(3) Sex-Linked Recessive Mutations.

Finally, the defects transmitted by sex-linked recessive alleles should be considered. Hemophilia, the Duchenne type of muscular dystrophy, and the partial color blindnesses (popularly referred to collectively as red-green color blindness) are adequately defined and of sufficient frequency of occurrence to have been properly investigated.[142] Each of these defects has

140. The total combined frequency of all of the above autosomal recessive diseases is approximately 30.8 per 100,000 births based on world-wide studies. Elimination of phenocopies could reduce their incidence. Their frequency would be about .03 per cent of births as contrasted with approximately 4 per cent for all diseases and defects with a genetic component. Based on the history of the revealed and published world-wide atomic energy program experience the probability of a person receiving an accidental or occupational acute exposure of 50 rads or more or a chronic exposure of 200 rads or more producing a child with any of the above recessive defects is exceedingly small. See U.N. SCIENTIFIC COMMITTEE 104 (frequency of autosomal recessive diseases in population) and 140-144 (analysis of past accidents on a world-wide basis). See also *Hearings on Employee Radiation Hazards and Workmen's Compensation Before the Subcommittee on Research and Development of the Joint Committee on Atomic Energy*, 86th Cong., 1st Sess., at 855-58 (1959) (summary of licensee radiation incidents). See also notes 134 *supra* and 146 *infra*.

141. See notes 64 and 70 *supra* and accompanying text.

142. See notes 18, 19, 20 *supra* and accompanying text for a discussion of sex-linkage and sex-linked traits. There are also sex-linked dominant traits, but proven ones are exceedingly rare in numbers and cases. See STERN 233-35.

Hemophilia is a constitutional abnormality of blood coagulation characterized by a life-long tendency to prolonged hemorrhage as well as markedly delayed coagulation time in affected males. Hemophilia A is due to a deficiency of a plasma factor (antihemophilic globulin-factor VIII) necessary for coagulation. Hemophilia B is a nearly identical disease but is the result of a deficiency of another necessary plasma coagulation factor (plasma thromboplastin component-factor IX). Other conditions greatly resemble hemophilia and result from deficiencies of other coagulation components or from circulating anticoagulants and must be differentiated from both hemophilia A and B which are the diseases transmitted by sex-linked recessive inheritance. See WINTROBE, CLINICAL HEMATOLOGY 861 (5th ed. 1961).

Duchenne type muscular dystrophy is a muscular disease appearing in children (usually in infancy) characterized by weakness and atrophy of the skeletal muscles with increasing disability and deformity as the disease progresses. This type is characterized by pseudo-hypertrophy of the muscles due to fat infiltration. See NELSON, TEXTBOOK OF PEDIATRICS 1268-69 (7th ed. 1959).

The partial color blindnesses are abnormalities in color vision in which the affected individual needs different intensity ratios of red:green:blue (primary colors) light to match white light (anomalous trichromosia) or needs only two of the three primary colors to match white (dichromasia). The genes producing these abnormalities are located on the X-chromosome and are recessive to the

been found to be clinically or physiologically heterogenous and the result of mutations at more than one locus.[143] Scientifically this creates a problem in using them as a marker for incidence of specific point mutations in a given population.[144] However, each represents a disease which is the result of a sex-linked recessive point mutation.[145] Consequently, the 50 rad acute and 200 rad chronic doubling doses would again be valid.

These defects would appear only in homozygous females which means that both the unexposed and the exposed parent would have to contribute the mutated gene. Consequently, given a definitively diagnosed female child with sufficient pedigree to verify the recessive sex-linked transmission, a more-probable-than-not test of causation could be met in cases in which either parent received more than the acute or long-term doubling dose, as in the cases of autosomal recessive mutations. Male offspring can inherit these X-linked defects only from their mother. Consequently, given a definitively diagnosed male child with sufficient pedigree to verify the recessive sex-linked transmission, a more-probable-than-not test of causation could be met in cases in which the mother received more than the acute or long-term doubling dose. As in the case of the autosomal recessive defects, the problem of contribution by an affected ancestor and transmission through "normal" carriers should be resolved by application of the substantial factor test.[146]

As with autosomal defects, these conclusions as to what is a doubling dose also are subject to the same qualifications arising from the fact that other preconception exposures to mutagenic

genes for normal color vision. See STERN 222-24. See STEVENSON 135-36. See also STERN 222-32.

Other sex-linked defects which individually are extremely rare and which present many of the difficulties referred to in note 129 *supra*, are certain types of congenital night blindness, a certain type of optic nerve atrophy, certain forms of hypogammaglobulinemia (the inability of the body to produce sufficient gamma globulin in the blood and sufficient antibodies to protect against bacterial infections), brown teeth, vitamin D-resistant rickets, and two types of diabetes insipidus (a condition not related to insulin deficiency in which the patient may void as many as 10 quarts of urine daily and require a similarly large intake of fluid). See STERN 232-33.

143. See U.N. SCIENTIFIC COMMITTEE 90 for a discussion of hemophilia and the Duchenne type of muscular dystrophy. All, or possibly all but one, of the X-linked partial color blindnesses fall into two different groups which are physiologically distinct. It is not known whether the common types of color blindness are controlled by four different genes at 2 or more loci in the X-chromosome or by different alleles at a single locus. STERN 226, 227.

144. See STEVENSON 125-37.

145. See STERN 222-38.

146. See note 138 *supra* and accompanying text.

agents may have occurred. In any event, again the occurrence of both hemophilia and the Duchenne type of muscular dystrophy is so rare that even if the number of first generation cases were doubled cases of females from sufficiently exposed parents and males from sufficiently exposed mothers would arise only once in many years.[147] Furthermore, hemophilia and Duchenne type of muscular dystrophy represent only a minute fraction of the potential harmful genetic impact of the exposure in question.[148]

On the other hand, the partial color blindnesses have been demonstrated in about nine percent of certain male populations and could constitute a large enough category to merit a special legal concept.[149] Even with color blindness, however, the frequency of occurrence, lack of pain or physical deformity, nonexistence of any medical treatment, and limited loss of capacity associated with these abnormalities should be taken into consideration in determining whether or not a special legal treatment is needed.

(4) Subsequent Generations.

The above discussions regarding specific diseases or defects dealt only with defects occurring in first generation offspring of exposed parents. In the case of fully penetrant dominant mutations, by definition, there is no problem of transmission of the harmful mutations to subsequent generations through pheno-

147. The combined total frequency of the hemophilias and of Duchenne muscular dystrophy accounts for only 4 in 10,000 births, on the basis of world-wide estimates. See U.N. SCIENTIFIC COMMITTEE 103 (Table V). For an estimate of the total exposures see notes 134 and 139 *supra*.

It should be noted that in the United Kingdom that for the various occupational groups monitored by the Radiological Protection Service (around 8,000 workers) excluding the small group engaged in X-ray crystallography (mean annual exposure too minute), the average annual doses ranged from 0.4 to 1.9 rads for men and 0.3 to 2.2 rads for women in 1959. The over-all average exposure for those monitored by the Atomic Energy Authority in 1959 (16,374 workers) averaged 0.42 rads. The highest doses recorded on individual films by the Radiological Protection Service in 1959 were 20 rads in 2 weeks for an industrial radiography worker and 5.4 rads in 2 weeks for a person engaged in administration of radiotherapy. In 1959 in the Atomic Energy Authority 3 rads in 13 weeks was exceeded in only 14 instances among over 16,000 workers continuously monitored by film badges. The highest doses accumulated by individuals employed by the Authority were 11.2, 11.3, and 10.7 rads. See *Second Report to the United Kingdom Medical Research Council, The Hazards to Man of Nuclear and Allied Radiations* 27-28, 120-26 (1960).

148. See notes 135 and 140 *supra*; see also notes 64 and 70 *supra* and accompanying text.

149. See STERN 226 (Waaler's 1927 study on secondary-school children in Oslo, Norway).

typically unaffected first-generation offspring; if causation cannot be proved in the first generation of offspring, it cannot be established at all. Both the autosomal and sex-linked recessive defects can be transmitted to subsequent generations through "normal" carriers; but it must be remembered that the genetic contribution of a given ancestor to any one generation of offspring decreases geometrically with each generation.[150] Consequently even larger exposures than those required for meeting the more-probable-than-not test for first generation defects would be required for defects in subsequent generations.

If because of the small number of cases that would arise, first generation specific defects should not be given special legal treatment, then those occurring in subsequent generations definitely should not.

c. Conclusions. — The enormity of the problem of proving causal connection in all of the genetic injury cases is compounded when consideration is given to the total number of complex diseases and defects which have some form of genetic basis and which may also result from harmful radiation-induced mutations. These range from shortened life-span due to arteriosclerotic heart disease occurring after the age of 45, to reduced resistance to infections, to "susceptibility" to malignancies, to many forms of mental disease, to minor physical defects, to gross congenital physical defects.[151]

When these complex proof problems must be applied by a judge and a jury in a specific case an almost impossible situation results. All of the above assumptions involve potential errors typically on the side of maximizing the risk of radiation-induced harm. They would have to be properly qualified if a fair presentation is made because it can be asserted safely that on the basis of the present state of medical, scientific, and genetic knowledge, the causal connection between a specific radiation exposure and a particular genetic injury is not capable of clear medical proof in the normal legal sense of the term.

An additional difficulty in proving causation is the necessity of determining, verifying, and presenting pedigree data. This would require obtaining birth certificates and full medical data and records of the affected individual's siblings (brothers and

150 See note 164 *infra* and accompanying text.
151. See RESEARCH COUNCIL (1956) 3-30; RESEARCH COUNCIL (1960) 3-24.

sisters) and lineal and collateral relatives (uncles, aunts, and cousins). To the extent possible, legitimacy also should be verified throughout the pedigree. Although as yet no scientific method of positive proof of legitimacy exists, blood groupings could be used to exclude certain members as illegitimate and to establish probabilities of legitimacy in some doubtful cases.[152]

In the light of all of these difficulties many if not most courts will quickly seize on the absence of any distinct biological, much less legal, entity in existence at the time of irradiation to deny recovery in all cases. The present writers would agree with this result (but not the reasoning), if the matter must be handled in the context of the ordinary personal injury trial in which reliance is placed upon the genetic sophistication of the medical profession generally and the ability of the court and jury to weed out dishonest claims and decide whether or not the more-probable-than-not proof test has been met.

Our concurrence in denial of recovery, however, should not be misinterpreted. The nonexistence of a separate biological and legal entity is not a good reason because, if recovery is denied, we *know* that many individuals, often through no fault of their own, will go through life uncompensated for the infirmity, inconvenience, and financial sacrifice caused by another's actions for which he would be legally liable but for the lack of an identifiable legal entity and specific proof of causal connection. Their loss will be no less painful, costly, or real because the wrongful impact occurred before conception. In a few cases, of course, where a defective offspring is born to parents at least one of whom has received a tripling or a doubling dose as the case may be, the radiation exposure can be proved more probably than not to have caused the defect, as pointed out above. These are the results that should be reached under the existing rules, but it is our position that the present system must be modified when applied to radiation injuries.

The real difficulty with permitting juries or even judges to deny or grant recovery on the more-probable-than-not basis is that the result will have only a fortuitous and purely coincidental correlation with the actual fact of causal connection in a particular case. All that can be proved is that if a group of sufficient size is exposed to radiation a larger number of off-

152. For a thorough discussion of blood-groupings from the standpoint of scientific evidence see McCormick, Evidence 377-83 (1954).

spring born to this group of individuals will have these diseases or defects than would be expected from the spontaneous rate; there is no way to determine specific causation in any one case. At least for some of these genetic injuries a much fairer system of tort compensation can be devised by use of a contingent injury fund which could make use of this very uncertainty, *i.e.*, the statistical nature of proof of causal connection.

In considering the need for a new approach, however, certainly the first question is the size of the affected group. The small number of additional cases of those category I a traits discussed above which would be caused by even 50 rads of radiation has been pointed out. From this the conclusion might be reached that nothing need be done. This is not a fair conclusion for at least two reasons. In the first place, the total number of defective individuals might be much greater than those with the rare category I a traits described above which will arise in the first generation. The damage over a number of generations could be truly significant and yet in most cases recovery will be denied. Secondly, within the next few years much more will be known about the possible genetic contribution radiation mutations will make for many other types of injuries than those discussed under category Ia. There is every reason to believe that the genetic contribution to other categories of traits, such as those in categories II and III, will be clarified. If it is established that radiation does make a substantial contribution to the production of such defects, the incidence rate will be much greater, perhaps as high as one or even several out of every 100 exposed persons.

It is important, therefore, to decide now what legal solution of this proof problem will be adopted. When our scientific knowledge is more certain, and as the use of radiation sources increases, genetic damage cases inevitably will arise in considerable numbers. In the meantime a statistical correlation system can be tried on the few cases that undoubtedly will arise even now. Much fairer results will be reached in these cases and the details of the proposal can be worked out before too many cases require adjudication.

Before making some preliminary and tentative suggestions about the contingent injury fund as applied to genetic injuries, however, one other consequence of potential deformed descendants should be considered.

C. *Recovery for Mental Distress Because of Fear of Having Defective Children*

Mental distress caused by fear of harm to their unborn children has been held to be a proper item of damages in cases involving injuries to pregnant women.[153] Recovery is for damage to the mother herself during the period of pregnancy and is not dependent upon the right of the fetus or embryo to recovery.[154] This apprehension of a pregnant woman that her unborn child might be injured is a proper element of damages even though it is established at the trial that such apprehension was unfounded or groundless and that plaintiff in fact gave birth to a normal, uninjured child.[155] Medical testimony to show that the feared result would probably follow from the injury is not necessary in order for the pregnant woman to recover.[156] The existence of this mental anguish is not disproved by evidence that if the plaintiff had been thoroughly versed in medical science she would have known that her fears were groundless; recovery is allowable if the fears are based on data that is scientifically untrue if such data is commonly believed by the general public.[157] The defendant's ignorance of the plaintiff's pregnant condition likewise will not defeat recovery.[158]

The question raised by the above decisions is whether or not by similar reasoning recovery should be allowed to irradiated parents who fear harmful mutational damage which might be expressed in their as-yet *unconceived* children. This irradiated person differs from the plaintiffs in decided cases — in which recovery was allowed — only by the absence of pregnancy.[159]

The question is whether or not this fear in the absence of pregnancy is so speculative an item that the law should not allow recovery. Although it is true that the fear in the pregnant woman is speculative, the fear in the case of the nonpregnant person is much more conjectural. In the case of the pregnant

153. Fink v. Dixon, 46 Wash. 2d 794, 285 P.2d 557 (1955); Fehely v. Senders, 170 Ore. 457, 135 P.2d 283 (1943); Prescott v. Robinson, 74 N.H. 460, 69 Atl. 522 (1908). See also Annot., 145 A.L.R. 1104 (1943) and cases cited therein; PROSSER, TORTS 178 (2d ed. 1955).

154. See note 153 *supra*.

155. Fehely v. Senders, 170 Ore. 457, 135 P.2d 283 (1943).

156. *Ibid.*

157. Annot., 145 A.L.R. 1104, 1112 (1943).

158. Prescott v. Robinson, 74 N.H. 460, 69 Atl. 522 (1908).

159. In Fehely v. Senders, 170 Ore. 457, 135 P.2d 283 (1943) the plaintiff was 6 months pregnant and in the *Prescott* case the plaintiff was pregnant but the duration of the pregnancy was not stated.

woman there is an existing condition which will terminate in the birth of a normal or abnormal child, or a miscarriage or stillbirth, all of which are actual possibilities, within a period of not more than nine months from the time of the impact. In the case of the nonpregnant person, pregnancy or prospective fatherhood itself is a matter of pure conjecture and might never take place for numerous reasons. Consequently, the law should not impose liability for this fear in the absence of pregnancy. To do otherwise would be to impose on an industry an unreasonable burden of liability to all persons exposed to radiation, including those who have not yet reached child-bearing age, for fear of a highly conjectural injury. This should be the case even though the potential harmful mutagenic effects of radiation have been the subject of great attention and frequent distortion, and in spite of the fact that much of the public has been led to believe, albeit erroneously, that all radiation causes mutations and that all of these mutations will result in grossly deformed children.[160]

III. RECOMMENDATION

The principal legal challenge which genetic injuries present is the development of a scientifically and juridically acceptable mechanism by which compensation can be provided. A contingent injury fund concept based on the statistically increased probability of acquiring a somatic radiation injury such as leukemia has been proposed as a solution for nongenetic damage cases.[161] The application of such a statistically based contingent

160. The press releases and newspaper editorials with regard to fall-out and the genetic effects of radiation are too numerous to list. They were particularly prolific in the fall of 1961 immediately after the U.S.S.R. resumed the atmospheric testing of nuclear weapons.

Some examples are N.Y. Times, May 15, 1961, p. 1, col. 3 (dental X-rays); N.Y. Times, Sept. 28, 1961, p. 17, col. 5 (nucleomitophobia); N.Y. Times, October 28, 1961, p. 7, col. 2-4 (Dr. Thomas Carlile); N.Y. Times, Nov. 6, 1961, p. 50, col. 1 (young react to fear of radiation); N.Y. Times, March 17, 1962, p. 1, col. 2-3 (fall-out debate — Mueller and Pauling).

With regard to the effect of news media information on cancer and a resulting cancerophobia the New York Court of Appeals said:

> "It is common knowledge among laymen and even more widely among laywomen that wounds which do not heal over long periods of time frequently become cancerous. Physical culture lectures to high school and college students, radio advice from life insurance companies, newspaper daily articles by doctors — all give the same advice."

Ferrara v. Galluchio, 5 N.Y.2d 16, 22, 152 N.E.2d 249, 252 (1958).

161. Estep, *Radiation Injuries and Statistics: The Need for a New Approach to Injury Litigation*, 59 MICH. L. REV. 259 (1960); Estep, *Radiation and the Law: with Emphasis on Damage and Proof Problems*, RADIOACTIVITY AND MAN 355-372 (1959). See *Hearings on H.R. 1267 and 2731 Before a Select Subcom-*

injury fund to genetic injuries, however, will be a much more complex matter.

Some of the complicating factors are absence of sufficient scientific knowledge to permit delineation of all genetic defects, the difficulty of determining the specific genetic mechanism and its connection with a specific harmful trait in a particular individual, the necessity in many cases of obtaining a verified pedigree to establish the mode of inheritance or acquisition of a particular defect, the multitude of injurious processes which have some genetic basis, the absence of a "doubling dose" which is quantitatively valid for all harmful mutations, and the absence of knowledge of the specific or general comparative human allele mutational radiation sensitivity. The fact that the great majority of the harmful mutants which would be produced would not be phenotypically expressed in the first generation offspring of the irradiated individual further complicates the situation. Nevertheless, a contingent injury fund concept which charges defendants at time of exposure but provides for compensation of exposed persons only when and if the injury manifests itself seems to be the only fair and equitable means of dealing with these injuries.

The specific administrative characteristics, details of funding, and relative feasibility of such a fund are beyond the scope of this present discussion, but will be the subject of further studies. However, because the present writers are so convinced that present legal rules will create such unfair results, something should be included here about the possibilities of using the contingent injury fund idea. Certain general considerations and characteristics which any contingent injury fund for genetic injuries must have are clear to us already.

Even though the linear theory of radiation mutation production is accepted, for legal purposes a radiation exposure cut-off point should be established. No offspring of an ancestor exposed to less than this amount would be eligible for compensation because the risk of increased harmful mutation from such exposures is inconsequential when compared to the genetic harm due to spontaneous mutations and induced mutations caused by other potential, but less understood, chemical, pharmacological, and dietary mutagens.[162] The doses of 50 rads for instantaneous

mittee on Labor of the House Committee on Education and Labor, 87th Cong., 2d Sess., at 234-49 (1962).

162. See STERN 517. See also notes 117-120 *supra* and accompanying text.

or acute exposures and 200 rads for long-term or chronic exposures seem to provide a cut-off point below which any exposures to a given individual should be regarded as statistically insignificant in specifically increasing the likelihood of an offspring in any subsequent generation bearing a harmful hereditary defect above the expected incidence of such defects resulting from spontaneous mutations or induced mutations caused by exposure to other potential mutagens.[163] Exposures below this level probably should be regarded as *de minimis* as far as the contingent injury fund is concerned. The maximum permissible exposures or recommended protection guides would not provide the proper cut-off point because they are not related to probability of injury but are in reality based on a need for regulatory action.[164] They are the doses below which one should be concerned with the application of only minimal protective measures for radiation control and above which one should apply increasingly strict controls of regulation because of the need to protect a whole population rather than an individual.

All diseases or defects which have a genetic component the incidence of which is influenced or maintained by gene mutation or chromosome aberration, regardless of the mode of inheritance, should be covered by the fund to the extent that reasonable scientific evidence of the relationship to radiation exists and that coverage is administratively feasible. Compensation should not be restricted to first generation offspring. On the other hand, the feasibility and administrative study of the fund concept should make specific recommendations as to any cut-off point regarding compensation to subsequent generations. In this connection, consideration must be given to the fact that with each generation that the affected descendant is removed from the exposed ancestor, there is a geometrically progressive decrease in the probability of causal connection to the particular irradiation.[165] The amount of pedigree information that a claim-

163. *Ibid.*

164. *Hearings on Radiation Protection Criteria and Standards: Their Basis and Use, Before Special Subcommittee on Radiation of the Joint Committee on Atomic Energy*, 86th Cong., 2d Sess., at 259 (1960). See also *id.* at 55, 61, 122, 258. Note that all of the occupational levels are designed for 50-year exposures. "But, worse than that, to use the maximum permissible dose as though it were a measure of injury makes it misleading." *Id.* at 249 (statement of Dr. R. R. Newell in a round-table discussion).

165. "We are prone to emphasize those genes which a child inherits from his parents. It is important not to forget the genes which he does *not* inherit. Of every pair of alleles a parent possesses, a child gets only one. As far as that child is concerned, the other allele is lost to the future, since segregation in meiosis

ant must present should also be determined in the course of the feasibility study. In any event, legitimate descent from an exposed ancestor must be established if gross errors are to be avoided.

Although there is no scientific basis for exclusion of many diseases and defects because many of the harmful mutational effects of radiation exposure will be the slight detrimentals with the smallest direct effect on any one generation or individual, certain genetic abnormalities would have to be excluded from compensation for reasons of feasibility of administration.[166] The diseases and defects to be covered by the fund should be determined by a competent legally-constituted body of physicians, geneticists, and lawyers. These determinations should be periodically reviewed and the list of specific diseases and defects to be covered should be appropriately revised when medically and genetically indicated. The use of a group of experts to make such determinations is preferable to use of courts and juries in the typical litigation context. If present procedures are used, inevitably in many, if not most cases, either scientifically unjustified windfalls or unfair denials of recovery will result.[167]

If accepted, the conclusions and recommendations here suggested could possibly lead to compensation for diseases or defects of many kinds, ranging from adult schizophrenia to obvious physical defects at birth, and may be thought to open a Pandora's box. Nevertheless, the contingent injury fund would seem to be the only fair solution to a legal problem which is

excluded it from the germ cells which led to the child's being. . . . Pride of ancestry is, at best, a questionable attitude, since an individual's value depends on himself rather than on properties of others. If the pride is based on the assumption that one has the same genes as a distinguished ancestor, it is well to remember that half of a person's genes are not transmitted to his child, and that this process of halving takes place in each generation." STERN 79. It should be noted that only half of an ancestor's *undesirable* genetic material reaches the next generation. See also STERN 517-18. This must not be confused with the factors governing expression which are substantially the same from one generation to the next. See note 122 *supra* and entire textual paragraph accompanying it.

166. See notes 69, 70 *supra* and accompanying text.

167. "Trying to prove for legal purposes the biological connection of irradiation with a particular nonspecific, latent injury under existing rules makes the 'correct' result theoretically impossible. Because radiation only increases the incidence of such injuries in an exposed group, is only one cause of many, and no way exists to distinguish those cases caused by radiation from those resulting from other forces, results reached in radiation cases under normal proof rules could best be described as a lottery. . . . Compensation will be granted to some unnecessarily and full recovery unjustly denied to others." *Hearings on H.R. 1267 and 2731, Before Select Subcommittee on Labor of House Committee on Education and Labor*, 87th Cong., at 2d Sess. 238 (1962) (referring to somatic injuries).

definitely emerging as the nuclear age progresses. Such a plan should be given serious consideration but first there must be definitive studies regarding details of administration, coverage, and funding. Legal scholars, practicing lawyers, and those government agencies responsible for the administration of the health and safety aspects of nuclear energy should assume responsibility for such efforts. The results of these studies might well have applicability not only here but also in other areas where legal systems and legal rules must solve new problems created by scientific and technological advances.