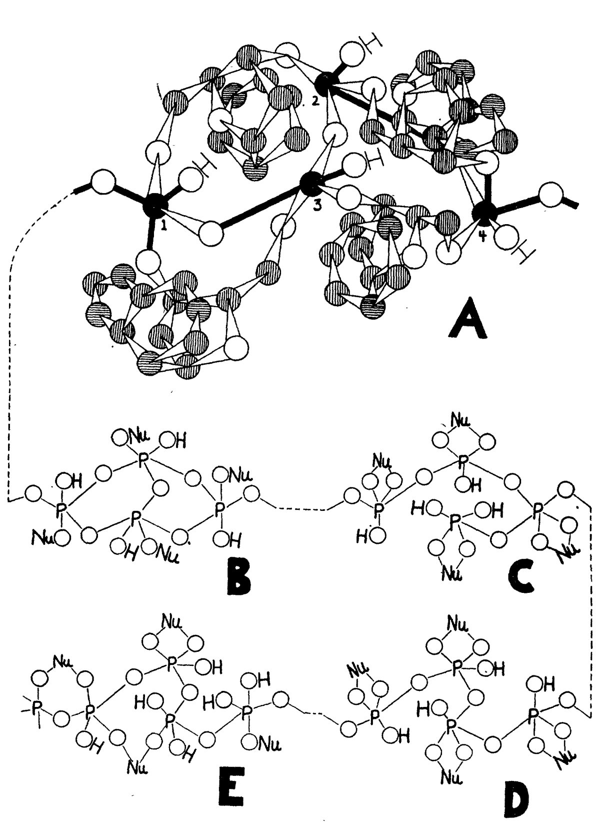

FIG. 1. The phospho-di-anhydride formula and variations of nucleic acid structure. *Section A*: closed circles, phosphorus atoms; open circles, oxygen atoms; vertical-lined circles, carbon atoms; and horizontal-lined circles, nitrogen atoms. Bond distances, bond angles, and relative atom and group sizes are not depicted exactly. The hydrogen atoms and other groups that are present on the bases and sugar moieties but which do not partake in the proposed bonding types have been omitted to avoid unnecessary confusion of the diagram.

Sections B, C, D, and E: the symbol Nu represents a nucleoside that is always shown in these diagrams as bound to the phosphorus atoms in phospho-ester linkages. Other atoms are conventionally designated.

dride structure having four primary dissociations for four P atoms and all nucleosides bound in cyclic anhydride linkages is pictured in Sec. D, Fig. 1. Then again, each unit half-cell may have a sprinkling of all types of linkages as diagrammed in Sec. E, Fig. 1. In this section there is also illustrated the linking of a nucleoside in a diphospho-ester grouping that ininvolves P atoms from adjacent unit half-cells. As another possibility for structural variation, a nucleic acid may have a combination of any and all of the unit half-cell types (Sec. A–E, Fig. 1) and others which are necessarily not shown.

Thus it is proposed that the structure of any nucleic acid is described by either the full phospho-di-anhydride or the full phospho-tri-anhydride formulas or as lying somewhere between these two extremes.

Considerations concerning end group types, branching, the unit cell structure and dimensions, titration data, the sequence of nucleosides, and the stability of nucleic acids that were previously applied to the phospho-tri-anhydride formula (*1*) are equally applicable.

The writer is indebted to C. Neuberg, Department of Chemistry, Polytechnic Institute of Brooklyn, for bringing to his attention the work of Anschutz (*5*).

The writer also wishes to thank the anonymous referee who pointed out that the purine to pentose link in part A of the figure is erroneously shown at position 3 as is the case for pentose-pyrimidine. He has always been aware of the work of the Gulland and Todd groups which established the point of linkage as position 9, but made an error in drawing the figure. The reader is urged to make a "mental" correction (rotate the purine portion approximately 180° in the same plane and bind at position 9), since the error in the diagram does not affect the basic backbone linkages that are proposed.

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A Comment on the Discussion of Genetics by His Holiness, Pius XII

SCIENCE, even theoretical science, has ceased to be the concern of a small number of devotees secluded in ivory towers. The ideological significance and the consequent importance in human affairs of certain branches of basic science have become widely recognized. The most telling recognition comes from leaders of human thought and action who are not themselves scientists but who feel called upon to concern themselves with problems of theoretical science and to state publicly their attitudes toward these problems. Genetics has been honored by such recognition more than any other biological discipline. It does not matter whether it was Stalin himself or some other communist dignitaries who decided that genetics is an evil product of bourgeois mentality, and that it must be replaced by Lysenko's version of old wives' tales. In either case, these busy men have paid genetics a wholly unintended compliment by expending considerable time and energy to delve into genetical problems.

A vastly greater honor is bestowed upon genetics by the statement of His Holiness, Pius XII, made on September 8, 1953, at the papal summer residence of Castel Gandolfo.[1] Geneticists will be pleased to have

[1] The text of the statement has been published, in original French, in *L'Osservatore Romano*, Sept. 9, 1953.

so high an authority recognize that "among diverse branches of biology, perhaps the most dynamic studies are those of genetics." It is even more gratifying that the aims of genetics " . . . attract an intense interest of institutions which occupy themselves with man as a moral personality, with his formation, and with his education which should fashion in him a mature and firm character, conscious of his responsibilities, of his method of thinking and of acting in matters that are decisive for the present as well as for eternity." And, indeed, "... philosophy can no longer disregard genetics if it wants to remain in contact with reality in its analysis of psychic activities."

The statement is carefully phrased and is hedged with the reservation that "this is what We should like to borrow from your branch [of science] without wishing to state Our own opinion." It opens with a succinct summary of the basic facts and concepts of genetics, which are said to be well-established positive attainments of science. The cell theory, fertilization, Mendel's laws, the gene theory, and mutation are thus passed in review. It is recognized that acquired traits and mutilations are not inherited, despite the contrary opinion of "Russian geneticists." The relationships between the genotype and the environment are rightly conceived to be dynamic ones, the genotype determining not rigid traits of the organism but rather its norm of reaction to the environment.

It comes, then, as a surprise that a much less hospitable view is taken of evolution. Evolution is certainly not denied, but it is admitted only as a possibility, as a hypothesis not yet verified, the opinion of some scientists which is not shared by others. One is left to wonder who are the "reputable scientists" who are said to have formulated "other hypotheses," and what these hypotheses are. Nor can one agree that the processes whereby one species may give rise to another still remain completely impenetrable. In all modesty and humility, and fully conscious of the admonition that one should not mistake hypotheses and opinions for established facts, a biologist may claim that he has at least some plausible models of how the origin of species may take place.

Moreover, it is factually incorrect to say that "one has not yet succeeded in making a species from another species." The scientific advisers of His Holiness have been guilty of negligence when they have failed to point out that the feat of obtaining a new species in experiment was accomplished more than a quarter of a century ago. The classical example is a completely new plant, *Raphanobrassica,* obtained through allopolyploidy. *Raphanobrassica* is a new species by any reasonable definition, since it is not only distinct in appearance but also reproductively isolated from its ancestors, and yet quite fertile with itself. In recent decades a fair number of new allopolyploid species have been brought into being, and what is more, some allopolyploid species existing in nature have been recreated in experiments.

It is, indeed, incontestable that we do not know the complete story of evolution and do not yet understand all the mechanisms which bring it about. Most biologists will be willing to go even farther and admit that, despite the great forward strides made in recent decades, the understanding of evolution is still in its infancy. The situation of evolution is, however, not appreciably different from that of other aspects of genetics. Assuredly there is much to be learned also about the mechanisms of the transmission of heredity.

To contrast our knowledge about the transmission of heredity as factual and well established with the knowledge about the occurrence of evolution as hypothetical and conjectural is not in accord with the present status of biological science. No less a geneticist than Goldschmidt still doubts that genes exist and proposes alternative hypotheses concerning this matter. Although Goldschmidt's skepticism is shared by very few of his colleagues, it will be recognized by many geneticists that the theory of the gene is going through a crisis. There is similar diversity of opinion concerning evolution, as is to be expected within a dynamic science during a period of rapid development. The course which the evolutionary process has taken in different groups of organisms (phylogeny), as well as the mechanisms which bring evolution about, are under investigation. But there can be no reasonable doubt of evolution as a historical fact, in the sense that evolution has taken place. This certainty includes the origin of man from nonhuman and prehuman ancestors, although the exact sequence of ancestral and collateral forms is far from adequately known, and the causation of the evolutionary events only dimly discerned. The occurrence of evolution in the history of the earth is well established as can be any event or process not witnessed by human observers, not witnessed for the simple reason that such observers did not yet exist or did not know how to record their testimony.

It is, of course, a fact that anti-evolutionists still exist, and that some Protestant religious denominations seem to be committed to fundamental views. Nor is it to be denied that, while a majority of anti-evolutionists are simply ignorant of the evidence which has led science to accept the evolutionary view of nature, a small minority hold anti-evolutionist opinions despite their being familiar with all the pertinent data. However, the existence of such informed anti-evolutionists is not a biological but rather a psychological problem. Informed anti-evolutionism is a phenomenon much like anti-geneticism of the Lysenko variety. In both cases the opposition arises from powerful emotional biases which make factual evidence and rational argument unable to change preconceived notions. The pronouncement made at Castel Gandolfo does not in any sense belong in this category, for it does not hold evolution to be contrary to or incompatible with Divine Revelation. But, regrettably, it does not show evidence of being well advised concerning the actual state of knowledge in biological science. Taking an over-conservative view in the matter of evolution makes the highest religious authority appear to oppose rather than encourage scientific progress. This is injurious both to science and to religion, keeping up several centuries of misunderstanding.

The concluding portion of the statement of Castel Gandolfo is concerned with practical applications of genetics. Having been addressed to the participants in the so-called "First Symposium on Medical Genetics," it naturally takes up the problem of defective heredity and its control. Geneticists will be gratified by the recognition that "the fundamental tendency of genetics and eugenics is to influence the transmission of hereditary factors in order to promote what is good and to eliminate what is harmful; this fundamental tendency is irreproachable from the moral point of view." Concerning the methods of accomplishing these ends, genetic counciling is endorsed. The carriers of bad heredity must be warned of the burdens which they are likely to impose upon themselves and their descendants. Eugenic sterilization is nevertheless opposed as a manifestation of "racism," which is explicitly rejected. However, when a carrier of a hereditary defect is incapable of conducting himself as a human being, one is justified in preventing him "in licit manner" from procreating new life. The statement closes with a reiteration that "the practical ends pursued by genetics are noble and worthy of being recognized and encouraged."

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A Jugular Technique for the Repeated Bleeding of Small Animals[1]

INVESTIGATORS in various fields have long been plagued by the problem of obtaining repeated blood samples from small laboratory animals. Mice, in particular, have presented just such a problem. To obtain repeated blood samples from the same mouse, a technique for bleeding from the external jugular vein has been developed and used in this laboratory. With the hope that such a technique may be of value to other investigators, an outline of the procedure follows.

[1] This technique was developed during the course of investigations supported by the Damon Runyon Memorial Fund for Cancer Research (grant No. 222).

Consistent success is dependent upon the animal being in the proper position for venipuncture. The animal is held by grasping the loose skin of the back firmly between the thumb and index finger of the left hand, and the ventral surface of the animal held upwards to expose the neck and upper thorax. Several threads of a 2 × 2 gauze sponge may then be caught on to the upper central incisors of the animal by pulling the taut edge of the sponge forward over the animal's mouth. This sponge is used to hold the head in hyperextension. When working alone, this position may be maintained by pulling the 2 × 2 gauze across the back of the hand and locking it between two fingers (Fig. 1*a*). In this hyperextended position, depilation from chin to mid-thorax is accomplished with little difficulty and exposes both external jugulars. These vessels are often distended and may be located without difficulty (Fig. 1*b*).

The puncture approach is determined, dependent upon the distention of the vessels, their size, etc. The needle (26 gage) and syringe should be wet with an anticoagulant. Immature animals, in which the jugulars are small, may be bled by introducing the needle 1- to 2-mm lateral to the sternoclavicular junction. At this point the expansion of the vessel, just cephalad to where it dips under the clavicle, may be visible as a blue, pulsating area. Fewer hemtomas were formed when the needle was introduced over the sternum, puncturing the skin 1 to 2 mm below the sternoclavicular junction, and the vessel approached in a caudocephalic direction (Fig. 1*c*). The blood is withdrawn slowly so as not to cause collapse of these small vessels.

Using this technique, it has been possible to obtain blood samples from weanling mice. Several older animals have been bled a total of twelve times within a

a b c

FIG. 1. (*a*) Mouse held in hyperextension to expose and dilate external jugular veins. (*b*) Dilated external jugular vein (see arrow). (*c*) Introduction of 26 gage needle into dilated external jugular vein (see arrow).