position of normal plasma (*11*). The isotopic excess in each plasma component was found to decline exponentially toward the average isotope concentration. In particular, the fractions of the plasma component isotopic excesses which interact daily are estimated at about 0.05, 0.5, 0.09, 0.06, and 0.09 for albumin, α-globulin, β-globulin, γ-globulin, and total plasma protein, respectively. Of the 0.09 value for total plasma protein only $1/T_1$, or about 0.036, could be attributed to plasma protein replacement from newly consumed protein.

On injecting dogs with tagged plasma protein, Yuile, Lamson, Miller, and Whipple obtained evidence of similar quick uptakes and subsequent interactions (*12*).

Also, the results estimated here for the various plasma components serve to illustrate the fact that all the other estimates are only averages of quantities having widely varying components.

Probably all the proteins that undergo the described interactions, as well as the relatively small amounts of nonprotein nitrogen, are the main constituents of the so-called nitrogen pool of the body.

References

1. SPRINSON, D., and RITTENBERG, D. *J. Biol. Chem.*, **180**, 715 (1949).
2. MAAS, A. R., LARSON, F. C., and GORDON, E. S. *Ibid.*, **177**. 209 (1949).
3. ROSE, W. C. *Federation Proc.*, **8**, 546 (1949).
4. SHEMIN, D., and RITTENBERG, D. *J. Biol. Chem.*, **153**, 401 (1944).
5. LONDON, I. M. Robert Gould Research Foundation *Symposia on Nutrition,* Vol. II, "Plasma Proteins," p. 71 (1950).
6. BOLE, W. F., *et al. J. Exptl. Med.*, **90**, 315 (1949).
7. SHEMIN, D., and RITTENBERG, D. *J. Biol. Chem.*, **166**, 627 (1946).
8. AMATUZIO, D. S., and EVANS, R. L. *Nature,* **171**, 797 (1953).
9. SPRINSON, D. *Isotopes in Biology and Medicine.* Madison, Wis.: Univ. of Wis. Press, 128, 1949.
10. AMATUZIO, D. S., *et al.* Unpublished results.
11. DOLE, V. P. *J. Clin. Invest.*, **23**, 708 (1944).
12. YUILE, C. L., *et al. J. Exptl. Med.*, **93**, 539 (1951).

Manuscript received August 5, 1953.

Comments and Communications

The Phospho-Di-Anhydride Formula and Its Relation to the General Structure of the Nucleic Acids

SINCE the publication of the author's originally proposed phospho-tri-anhydride structure for the nucleic acids (*1*), Markham and Smith (*2*) have reported that both mono- and di-nucleotides possessing cyclic anhydride linkages and phospho-di-ester dinucleotides were products of the enzymatic degradation of yeast ribonucleic acid. Further, Cohn and Volkin (*3*) have succeeded in demonstrating the presence of 5-phospho-nucleotides in the digest of calf liver ribonucleic acid, which in itself is not incompatible with the phospho-tri-anhydride structure. More recently, Merrifield and Woolley (*4*) have presented conclusive evidence for the presence in yeast ribonucleic acid of "dinucleotides having two phospho-sugar ester bonds on one nucleoside and dinucleoside phosphates which have two nucleosides attached to one phosphate." These authors, aware only of the tri-anhydride structure, have concluded that their results ". . . do not seem to conform to the structure recently proposed by Ronwin." This conclusion is justified only when consideration is narrowed to the special case of the phospho-tri-anhydride structure (*1*); however, the results of these authors, together with those of the others mentioned above, are quite compatible with the amplified form of the P-O anhydride polymer core formula that is being presented here.

In addition, the author has recently become aware of the earlier synthesis of compounds possessing five oxygen atoms bound to a single phosphorus atom (*5*), which provides a precedent for the anhydride types that are proposed. The amplification is assisted diagrammatically by Fig. 1.

Section A is essentially one-half a unit cell for a phospho-di-anhydride structure for the nucleic acids along the same pattern as the previously proposed phospho-tri-anhydride structure (*1*). It is to be noted that all the nucleosides are depicted as engaged in diphospho-ester linkages that can give rise to such products as described by Merrifield and Woolley (*4*) and Markham and Smith (*2*). Each phosphorus atom carries one primary dissociation. Were the bond, P_2-O-P_3 of Sec. A, Fig. 1 hydrated, there would result two secondary dissociations in addition to the four primary dissociations already shown. This condition would split the P to O polymer core, but the chain would still be intact. Though the bases are pictured as parallel, but not coplanar to the sugar moieties (only the nuclei are shown), in accordance with Astbury's description (*6, 7*), they may be and probably are perpendicular to the D-ribose rings as recently reported for cytidine by Furberg (*8, 9*).

All the half-cells of any nucleic acid (either the ribo- or desoxyribo types) may possess the structure shown in Sec. A, Fig. 1 (the phospho-di-anhydride type) or they may all conform to the originally proposed phospho-tri-anhydride formula (Sec. B, Fig. 1) in which all the nucleosides are mono-esterified. As another condition, they may all assume the phospho-di-anhydride core wherein the nucleosides are bound as cyclic anhydrides (*2*) as depicted in Sec. C, Fig. 1. In this case, there is illustrated a situation in which three primary and one secondary dissociations are present for four P atoms. Another type of di-anhy-

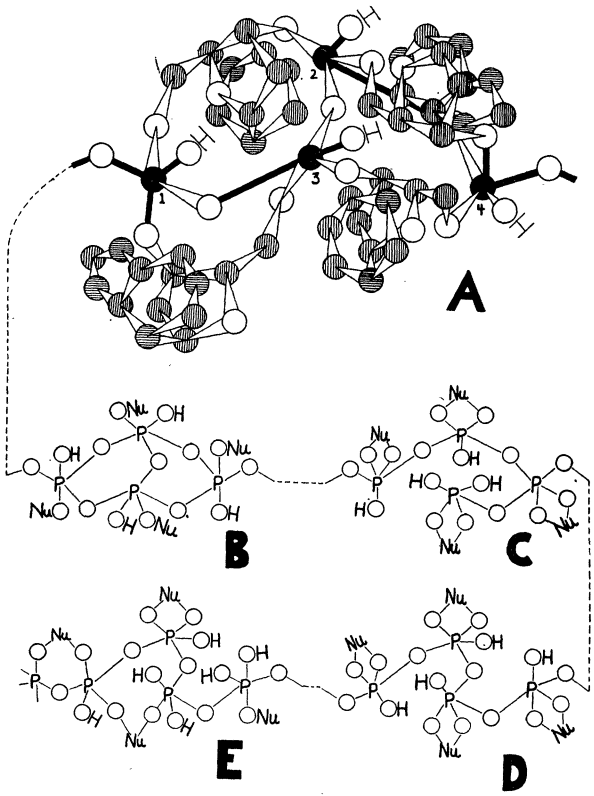

FIG. 1. The phospho-di-anhydride formula and variations of nucleic acid structure. *Section A*: closed circles, phosphorus atoms; open circles, oxygen atoms; vertical-lined circles, carbon atoms; and horizontal-lined circles, nitrogen atoms. Bond distances, bond angles, and relative atom and group sizes 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 involves 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.

EDWARD RONWIN[1]

Department of Chemistry
Iowa State College

References

1. RONWIN, E. *J. Am. Chem. Soc.*, **73**, 5141 (1951).
2. MARKHAM, R., and SMITH, J. D. *Nature*, **168**, 406 (1951).
3. COHN, W. E., and VOLKIN, E. *Ibid.*, **167**, 483 (1951).
4. MERRIFIELD, R. B., and WOOLLEY, D. W. *J. Biol. Chem.*, **197**, 521 (1952).
5. ANSCHUTZ, L. *Ann.*, **454**, 116 (1927).
6. ASTBURY, W. T. *Symposia Soc. Exptl. Biol.*, **1**, 66 (1947).
7. ASTBURY, W. T., and BELL, F. O. *Cold Spring Harbor Symposia Quant. Biol.*, **6**, 109 (1938).
8. FURBERG, S. *Acta Chem. Scand.*, **4**, 751 (1950).
9. ———. *Acta Cryst.*, **3**, 325 (1950).

[1] Present address: Department of Physiology, Tufts Medical College, Boston 11, Mass.

Received June 8, 1953.

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.