

cent of the norm would be heterozygous for the abnormal gene. Whether the small amount of  $\alpha_1$ -antitrypsin found in the affected homozygotes is structurally normal must await further study.

In view of the apparent innocuous nature of the gene in single dose, an attempt was made to estimate the frequency of the trait in a random population by surveying 193 whites from a community in Georgia (9); all serums were examined by starch-gel electrophoresis. Diminution in intensity of the  $\alpha_1$ -antitrypsin band was further investigated by quantitative determination of the serum  $\alpha_1$ -antitrypsin activity. All serums were examined by both methods, but it became apparent that the starch-gel-electrophoretic technique alone was a fairly reliable screening method for detecting deficiency of this protein (Fig. 3). Four of the 193 individuals studied had serum  $\alpha_1$ -antitrypsin concentrations approximately 50 percent of the norm ( $342 \pm 78.5 \mu\text{g}$  of trypsin inhibited by 1 ml of serum); they corresponded to a heterozygous frequency of the trait of 2.1 percent. The calculated homozygous frequency in this small sample of the population is approximately 1 per 10,000 (this estimate is necessarily very provisional). Further

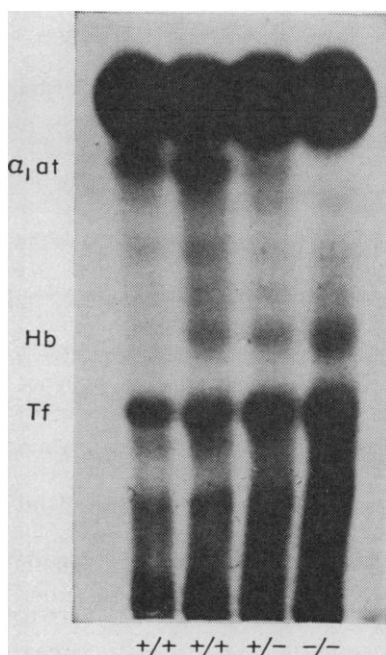


Fig. 3. Genetic variants of the serum  $\alpha_1$ -antitrypsin. Starch-gel electrophoresis of two normal serums (+/+), one heterozygote (+/-), and one homozygous deficient individual (-/-). Note the decrease in intensity of the  $\alpha_1$ -antitrypsin band ( $\alpha_1\text{at}$ ) in +/- and -/- individuals. Hb, free hemoglobin; Tf, transferrin.

studies in several populations will be required to establish variations in frequency of this serum polymorphism and to elucidate the possible relation of serum  $\alpha_1$ -antitrypsin deficiency to certain types of pulmonary emphysema.

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#### References and Notes

1. L. Camus and E. Glay, *Compt. Rend. Soc. Biol.* **49**, 825 (1897).
2. H. E. Schultze, N. Heimburger, K. Heide, H. Haupt, K. Störko, H. G. Schwick, in

- Proc. 9th Congr. Europ. Soc. Haematologists*, Lisbon, 1963 (Karger, New York, 1963), p. 1315; F. Kueppers and A. G. Bearn, unpublished observations; W. Mehl, W. O'Connell, J. DeGroat, *Science* **145**, 821 (1964).
3. H. E. Schultze, K. Heide, H. Haupt, *Klin. Wochschr.* **40**, 427 (1962).
  4. C.-B. Laurell and S. Erikson, *Scand. J. Clin. Lab. Invest.* **15**, 132 (1963).
  5. S. Erikson, *Acta Med. Scand.* **175**, 197 (1964).
  6. M. Bier, in *Electrophoresis*, C. Wunderly, Ed. (Academic Press, New York, 1959), p. 186.
  7. N. Heimburger and H. G. Schwick, *Thromb. Diath. Haemorrh.* **7**, 432 (1962).
  8. B. F. Erlanger, N. Kokowsky, W. Cohen, *Arch. Biochem. Biophys.* **95**, 271 (1961).
  9. The serum samples were supplied by Dr. C. Hames, Claxton, Georgia. Work supported in part by PHS grant 5T1GM 577 and H3341 from the National Institute of General Medical Sciences, and by grant U-1067 from the Health Research Council of the City of New York. We thank Drs. A. Cournand, J. H. McClement, J. B. Cromie, and A. Davis for the opportunity to study the Bellevue Hospital patients.

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### Serum Albumin: Polymorphism in Man

**Abstract.** Serums from 1015 individuals, mainly Norwegians, were studied by starch-gel electrophoresis. All but one showed the same albumin phenotype. The appearance of the exceptional sample on starch gel fits with that of a heterozygote. A genetic theory of two alleles  $Al^F$  and  $Al^S$  is proposed.

Several examples of a genetically determined condition in man, usually called abnormal bisalbuminemia, have been reported (1, 2, 3). This condition is characterized by two serum albumin zones instead of the usual one. In animals such as horses (4, 5), cattle, sheep, pigs (4), and chickens (6) similar variations in the albumin have been observed. However, in most animal species three phenotypes are found showing distributions fitting with a genetic theory of two alleles which have been named  $Al^F$  and  $Al^S$  (4, 6). In connection with investigations of albumin polymorphism in domestic species we have carried out comparative studies of human albumin and now report results on serum albumin polymorphism in man.

A total of 1015 serums were investigated, 800 of them from pregnant women living in various parts of Norway. Two hundred samples came from seamen of whom 75 percent were Norwegians, and 15 came from Africans in a Congo hospital.

Albumin types were determined by starch-gel electrophoresis, using a method based upon Poulik's (7) horizontal discontinuous system. The serum samples were diluted 1:3 with distilled water, and the pH of the gel buffer was usually 7.8. No other details are given because separation of the major albumin fractions is easy with ordinary electrophoretic methods.

Two phenotypes were observed (Fig. 1). The common type designated FF appears as a major band with a very weak one in front. Separation of al-

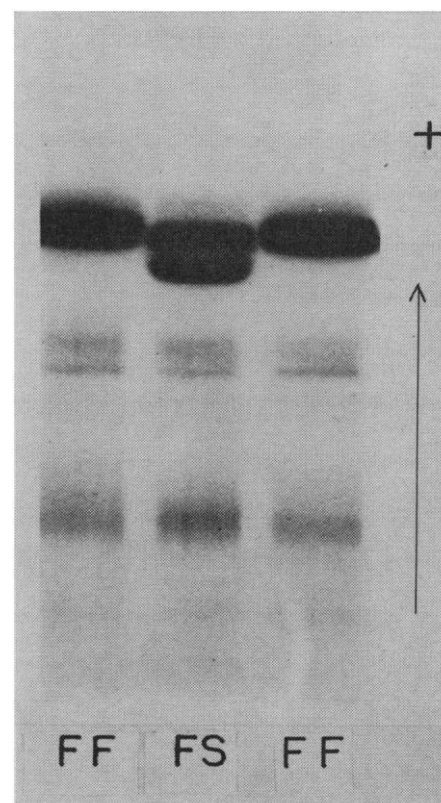


Fig. 1. Gel stained with amido black, showing three electrophoretic patterns of two albumin phenotypes. The origin is at the base.

bumin fractions can take place in both alkaline and acid buffer systems (pH 5.9). There is some further indication that the major bands in the FF and FS phenotypes are each composed of two bands, but we have not always obtained separation of these.

The other phenotype, FS, was found in only one individual, a woman living in southern Norway. Her albumin type appears as two major bands with a very weak one in front. Compared to the zones of the FF phenotype, the FS type shows about half the staining intensity and thickness of bands.

These results indicate a theory of two codominant alleles. The very rare heterozygote is most probably the same as the bisalbuminemia already described. We consider this heterozygosity to be a quite normal condition and another example of a polymorphic serum protein system of which many are now known in the animal kingdom. We prefer to call the two alleles  $Al^F$  and  $Al^S$  (F, fast; S, slow). This nomenclature will have advantages

over  $A_1$  and  $A_2$  (2) and A and B (3) if additional alleles are found.

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#### References and Notes

1. H. Bennhold, T. Ott, G. Scheurlen, *Verhandl. Deut. Ges. Inn. Med.* **64**, 279 (1958); F. Wuhrmann, *Schweiz. Med. Wochschr.* **89**, 150 (1958); H. J. Nennstiel and T. Becht, *Klin. Wochschr.* **35**, 689 (1957); G. Franglen, N. H. Martin, T. Hargreaves, M. J. H. Smith, D. I. Williams, *Lancet* **I-1960**, 307 (1960); P. L. Adner and A. Redfors, *Nord. Med.* **65**, 623 (1961).
2. M. Knedel, *Clin. Chim. Acta* **3**, 72 (1958).
3. D. P. Earle, M. P. Hutt, K. Schmid, D. Gitlin, *J. Clin. Invest.* **38**, 1412 (1959).
4. M. Braend and G. Efremov, *Proc. Intern. Congr. Animal Reproduction and Artificial Insemination*, 5th, Trento, Italy, September 1964.
5. C. Stormont and Y. Suzuki, *Proc. Soc. Exptl. Biol. Med.* **114**, 673 (1963).
6. W. M. McIndoe, *Nature* **195**, 353 (1962).
7. M. D. Poulik, *ibid.* **180**, 1477 (1957).
8. We thank O. Hartmann (State Institute for Public Health), K. J. Lindqvist (Veterinary Institute), and P. Lund Larsen, all of Oslo, for providing samples. Supported in part by grants from the Agricultural Research Council of Norway. One of us (G.E.) is on leave from the Department of Physiology, University of Skopje, Yugoslavia, with a scholarship from the Royal Norwegian Ministry of Foreign Affairs.

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## Purine and Pyrimidines in Sediments from the Experimental Mohole

**Abstract.** Cytosine, adenine, guanine, and thymine, but not uracil, have been detected in core samples taken from various depths of the experimental Mohole. The following quantities of bases were found in the deepest core samples available (approximately  $25 \times 10^6$  years old): cytosine, 2.5  $\mu\text{g}/5$  g; adenine, 0.9  $\mu\text{g}/5$  g; guanine, 0.2  $\mu\text{g}/5$  g; thymine and uracil, 0  $\mu\text{g}/5$  g.

The existence and composition of organic compounds of biological origin in fossils, sediments, and sedimentary rocks provide clues for the understanding of biological evolution and the origin of life. Most reports on biogeochemical analysis have been concerned with hydrocarbons, amino acids, sugars, and porphyrins (1). Although

the role of nucleic acids as the genetic material in all known forms of life is clearly established, the quantities of nucleic acid residues as paleobiochemicals have not previously been reported. Nucleic acid residues have been qualitatively found in recent sediments and various fossils (2). I report here an analysis of purine and

pyrimidine bases in core samples obtained from the experimental Mohole drilling during March and April 1961 off Guadalupe Island, Mexico (3). The deepest core sample available, EM 7-3, has been estimated to be  $25 \times 10^6$  years old (4). A detailed study of the biogeochemistry of sediments in the experimental Mohole has been reported (5).

Since the usual methods of extracting nucleic acids from biological materials and determining the base composition were not applicable to the largely inorganic core samples, the following procedure was developed. The purine and pyrimidine bases were extracted from the sediments after hydrolysis in 12N perchloric acid at 100°C for 1 hour. The bases were separated from the highly saline extracts by adsorption onto activated charcoal-celite and eluted with 2 percent (by volume) of concentrated ammonium hydroxide in 50 percent (by volume) aqueous ethanol. The extracts were further purified and characterized by two-dimensional chromatography on Whatman No. 40 paper by the descending technique, the chromatogram being developed first with a mixture of isopropanol and hydrochloric acid (6), and then with *n*-butanol and ammonia (7). The bases were identified, and the quantities were estimated by the characteristic ultraviolet absorption spectra in both acid and alkali. The degree of ultraviolet-absorbing materials in all the reagents used was established by appropriate controls. To determine the efficiency of the analytical procedures, radioactive bases were added prior to hydrolysis of the sediment. The recovery of each base was established from the fraction of initial radioactivity found in the isolated base (8). This method does not distinguish the free bases from those present as nucleosides or nucleic acids.

Table 1 shows the quantities (uncorrected for losses) of the five naturally-occurring bases found in core samples taken from various depths. If corrected for recovery, the quantities of pyrimidines in the core samples would be approximately twice those reported in Table 1. The corrected quantities of adenine and guanine in the sediments are difficult to estimate accurately because of the low recovery of these purines. Although recovery of all three pyrimidines was more than 40 percent, only cytosine was found at all depths.

Table 1. Quantities of purines and pyrimidines in the experimental Mohole sediments ( $\mu\text{g}/5$  g dry weight). The average recovery (percent) of base was as follows: cytosine, 43; adenine, 10; guanine, 5; thymine, 45; uracil, 49. The quantities reported have not been corrected for losses during the analytical procedures.

Sample	Depth (m)	Cytosine	Adenine	Guanine	Thymine	Uracil
L-66	0	5.2	3.5	6.5	1.2	0
EM 7-7	0	2.3	2.0	3.5	1.0	0
EM 6-2	76	3.2	0.6	2.5	0	0
EM 8-11	101	0.8	2.5	0.5	0	0
EM 8-14	129	1.2	0.5	0.5	1.4	0
EM 7-3	170	2.5	0.9	0.2	0	0