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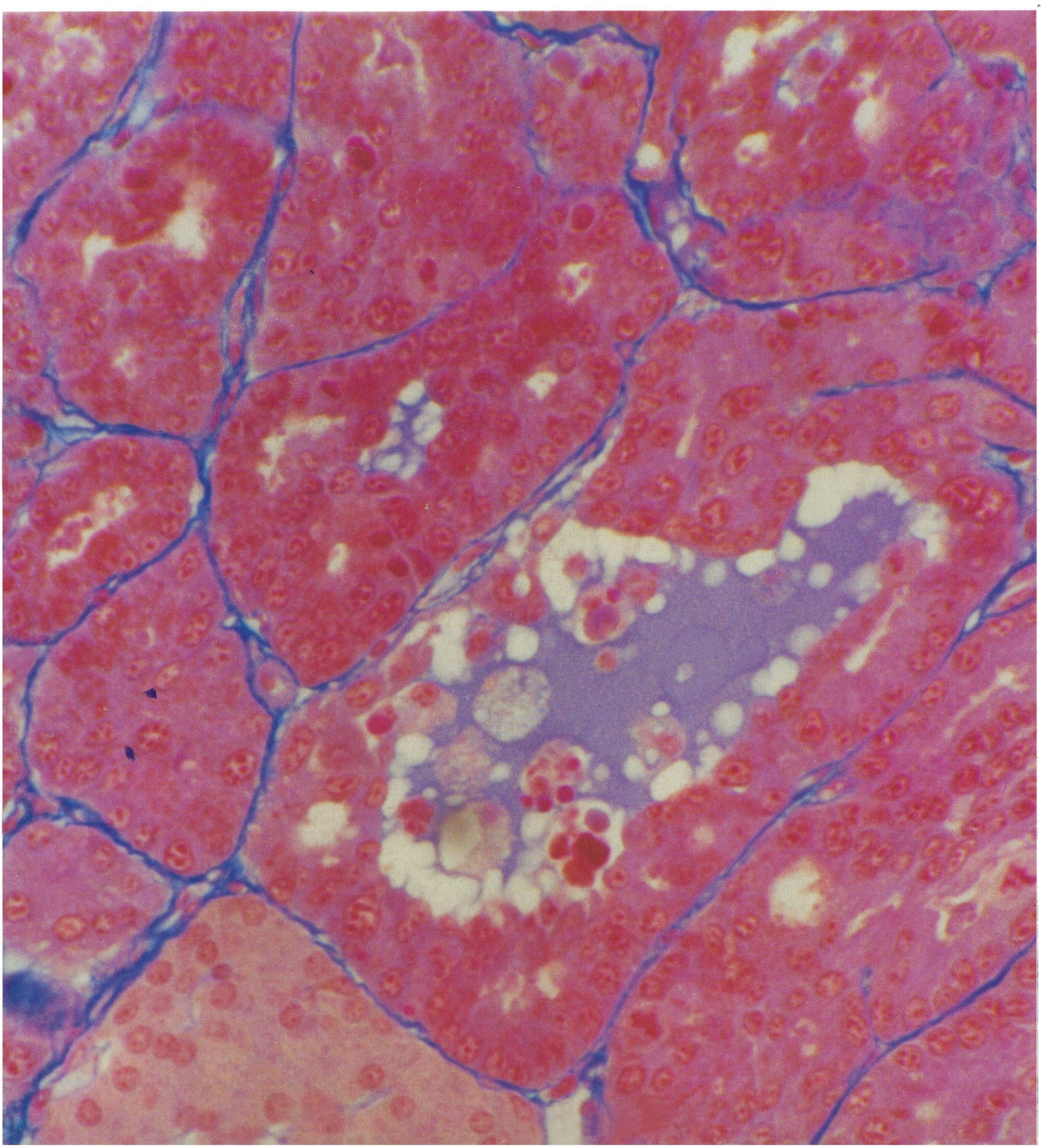

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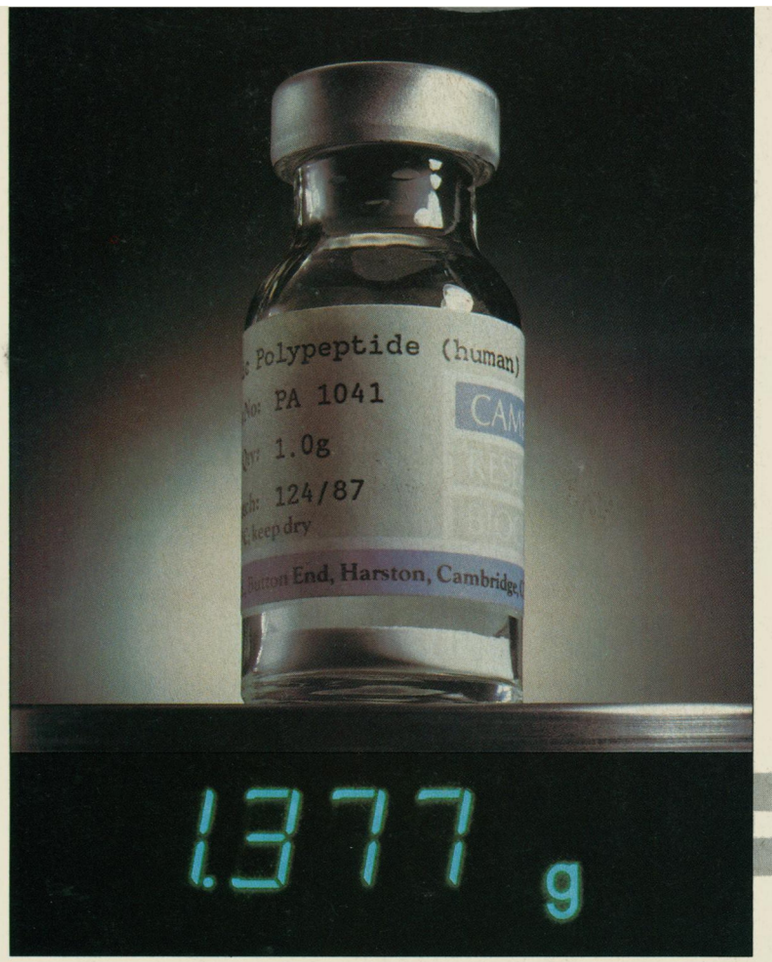

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COVER Photomicrograph of pancreas from 8½-week-old transgenic mouse carrying an elastase-SV40 gene, stained with Heidenhain's Aniline Blue. A normal islet is adjacent to hypercellular and dysplastic acini, representing a preneoplastic stage associated with expression of SV40 large T antigen in exocrine cells (magnification, about ×800). See page 188. [Albee Messing, School of Veterinary Medicine, University of Wisconsin-Madison, Madison, WI 53706]

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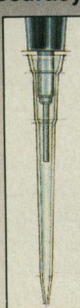

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Meteorites from asteroids

THE asteroid belt (situated between Mars and Jupiter) may be the source of carbonaceous chondrites, the oldest known meteorites; these contain materials from which asteroids and planets are thought to have formed (page 183). A comparison of the infrared absorption spectrum of asteroid 130 Elektra with the spectrum of one of the 40-odd carbonaceous chondritic meteorites found on the earth—the well-studied Murchison meteorite—supports the notion of an asteroid origin for this rock. Cruikshank and Brown used the cooled-grating array spectrometer at Mauna Kea to study the asteroid and a laboratory reflectance spectrometer to study extracted organics from the Murchison meteorite; at a wavelength of 3.4 micrometers, an absorption band of hydrocarbons, there is general correspondence in signatures of the two. The Murchison meteorite contains amino acids, alkanes, purines, and other complex organic compounds; it is not yet possible to say which are or are not components of 130 Elektra. The spectral analysis does show that distant regions of the solar system contain complex organic compounds.

Origin of human colorectal cancers

TUMORS in the colon and rectum appear to develop from unchecked proliferation of single cells: early in the expansion into a clone, a small benign adenoma may form, but, with further proliferation and activations and inactivations of specific genes, a large, malignant, invasive carcinoma can develop (page 193). This scenario is proposed by Fearon *et al.* who analyzed the clonal compositions of and loss of chromosome pieces from 50 colorectal tumors from 20 women. The monoclonal nature of the tumors was established by evaluation of X chromosomes in tumor cells: in any one tumor, every cell had the same active X chromosome, whereas in normal tissue from the same individual a mosaic of active X chromosomes is standard. In most (76%) of the carcinomas, a piece of chromosome 17 (called 17p) had been lost; most adenomas retained 17p. In two tumors containing both adenoma and carcinoma elements, only carcinoma-associated cells lost 17p; in a third tumor that showed more extensive abnormal development, both adenoma and carcinoma lacked 17p. The conversion from adenoma to carcinoma thus appears to coincide with loss of 17p and, within this chromosomal region, a tumor suppressor sequence probably resides.

Classifying plant pathogens

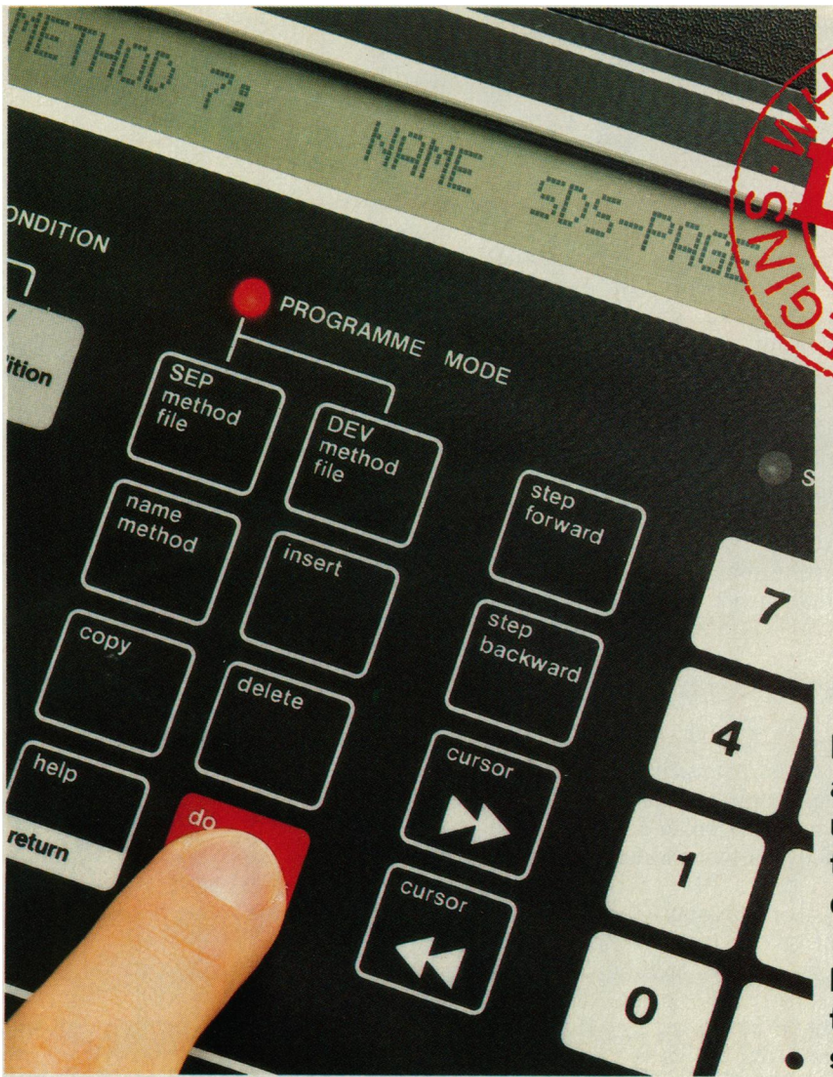
YIELDS of peach and cherry crops are sometimes drastically reduced by Western X-disease, which is caused by a mycoplasma-like organism (MLO) (page 197). MLOs are transmitted from phloem (food-conducting vessels) of one plant to phloem of another by phloem-feeding leafhoppers. More than 200 plant diseases are thought to be caused by MLOs and to be transferred by insect vectors (which also develop disease); the number of different MLOs involved is unknown because techniques have not been available for distinguishing among the (morphologically indistinguishable) MLOs. Kirkpatrick *et al.* describe strategies for isolating and cloning MLO DNA from vector leafhoppers and for assessing the relatedness of MLO DNA in plants and insects in the laboratory and in the field. The new DNA probes and recombinant techniques should be useful for studying different diseases and their agents, for distinguishing among them, and for identifying natural reservoirs of MLOs.

Unusual amino acid in frog peptide

AMPHIBIANS have numerous peptides in their skin that are comparable in their actions to mammalian hormones and neurotransmitters (page 200). One of these is dermorphin, an abundant opioid found in South American tree frogs. Dermorphin consists of only seven amino acids, the second of which is unusual because it is an alanine in the D-configuration; this is one of the few reported examples of a D-amino acid in an animal peptide. Richter *et al.* isolated messenger RNA from the skin of frogs caught in Argentina, prepared and cloned DNA from it, and screened the DNA for sequences encoding the dermorphin-specific heptapeptide. Unexpectedly, information within the DNA specified the production of the L-isomer of alanine at position 2 and not the D-isomer. Therefore, after the peptide is synthesized, there must exist a mechanism for converting L-alanine to D-alanine. A search can begin for enzymes that bring about this conversion and for other animal peptides that contain D-amino acids.

Inherited bleeding disorder

NORMALLY, the protein α_2-antiplasmin (α_2-AP) inhibits the action of plasmin (a clot-dissolving substance); however, in two children in a family from the city of Enschede in the Netherlands, α_2-AP acts as a substrate for plasmin, and the children suffer from a serious bleeding disorder, α_2-AP Enschede (page 209). The siblings and their parents were studied by Holmes *et al.*; the parents proved to be heterozygotes, and the two children were homozygotes for the α_2-AP gene. All four family members had normal levels of α_2-AP; the molecules retained 50% of the normal level of activity in the parents and were inactive in the children. Through DNA sequence analyses, a three-base-pair insertion was identified in the α_2-AP Enschede gene that resulted in addition of alanine near the molecule's reactive site. Experimental insertion of alanine at the same site in a normal α_2-AP molecule abolished plasmin-inhibitory activity and converted the molecule into a substrate for plasmin. Structure-function relations disclosed for α_2-AP may apply to related proteins of the serine protease inhibitor superfamily to which this molecule belongs.



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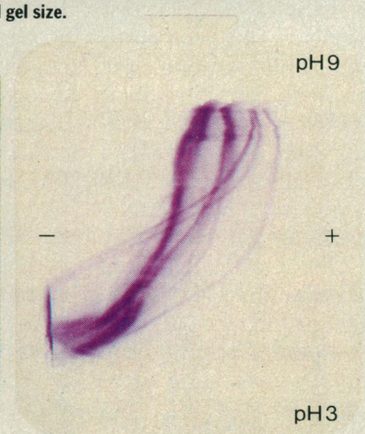

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Ozone and Acid Rain

Some level of deleterious effects of ozone, photochemical oxidants, and acid rain probably will be present for a long time. There will be no quick fixes. The phenomena involved in converting SO_2 and NO into more toxic substances are complex. Without understanding such phenomena and without knowledge to permit establishing realistic priorities on what needs to be curtailed and where, the United States could spend hundreds of billions of dollars ineffectively.

Congress was wise when in 1980 it mandated a major National Acid Precipitation Assessment Program (NAPAP). The activity involves 12 federal agencies and has a current annual budget of $85 million. Congress stipulated that efforts include programs to yield information about many aspects of acid rain. Examples are identification of sources, establishment of monitoring networks, research in atmospheric physics and chemistry, methods of controlling emissions, and identification of areas at risk. The program has led to publication of more than 1000 papers in peer-reviewed journals. It has also resulted in a recently issued interim report on acid precipitation.* The report consists of four volumes containing about 900 pages and a total bibliography of 1600 references. Preparation of the report, which is well-written, involved many authors and extensive peer reviews. The content is largely limited to research and observations performed in the United States.

In the discussion that follows, the emphasis is on the important roles of ozone and other oxidizing agents. The major polluting emissions are SO_2, NO, and volatile organic chemicals. In the usual ambient concentrations, these substances are relatively harmless. However, when SO_2 and NO are oxidized, they are converted into more acid, more toxic, substances. Oxidants, including OH, H_2O_2, HO_2, and organic peroxides, arise out of complex photochemistry that involves the ozone, the nitrogen oxides, and volatile organic chemicals. Were SO_2 the only pollutant, most of it would escape unchanged to the western Atlantic Ocean where it would be so diluted as to have no effect. At present about 35 percent of the SO_2 produced in the United States leaves the continent. In contrast, because of higher rates of reaction with oxidants, most of the NO is converted into nitric acid and deposited on land.

The nitrogen oxides are involved in the production of ozone, some of which is naturally present. But particularly in urban settings where concentrations of NO_x are elevated and volatile organic chemicals such as those in gasoline are present, ozone concentrations may rise to levels deleterious to health. The Environmental Protection Agency has set standards for levels not to be exceeded, but nearly half of urban communities are not in compliance. The NO_x involved in the formation of urban ozone comes mostly from vehicular emissions.

Ozone is toxic to plants, as has been shown by greenhouse experiments. Annually, ozone is thought to be responsible for more than $1 billion worth of damage to agricultural crops. Near Los Angeles, ozone and photochemical oxidants have damaged forests in the San Bernardino mountains. Extensive damage to trees high in the Appalachians is probably due to additive effects of ozone, oxidants, and very acid fog and rain. In the damage to forests, natural organic chemicals such as terpenes emitted from trees undoubtedly have important roles. The quantities of volatile chemicals emitted during the summer by vegetation exceeds those from anthropogenic sources.

In the past, efforts to abate air pollution have emphasized curtailment of SO_2 emissions. As a result, these have been reduced 27 percent. Comparable reduction of NO has not been achieved. Auto emissions have been reduced somewhat, but total NO from trucks has increased. Most of the reduction of SO_2 emissions was achieved by flue gas desulfurization at utility plants. That process is not effective in removing NO. A shift to more emphasis on the curtailment of emissions of NO seems necessary. Excellent technology for reducing NO emissions from new utility plants is now available. The problem of reducing NO from vehicles is more difficult and might require a costly program to replace gasoline by methanol as a motor fuel.—PHILIP H. ABELSON

*National Acid Precipitation Assessment Program, *Interim Assessment, The Causes and Effects of Acid Deposition* (Government Printing Office, Washington, DC, 1987).

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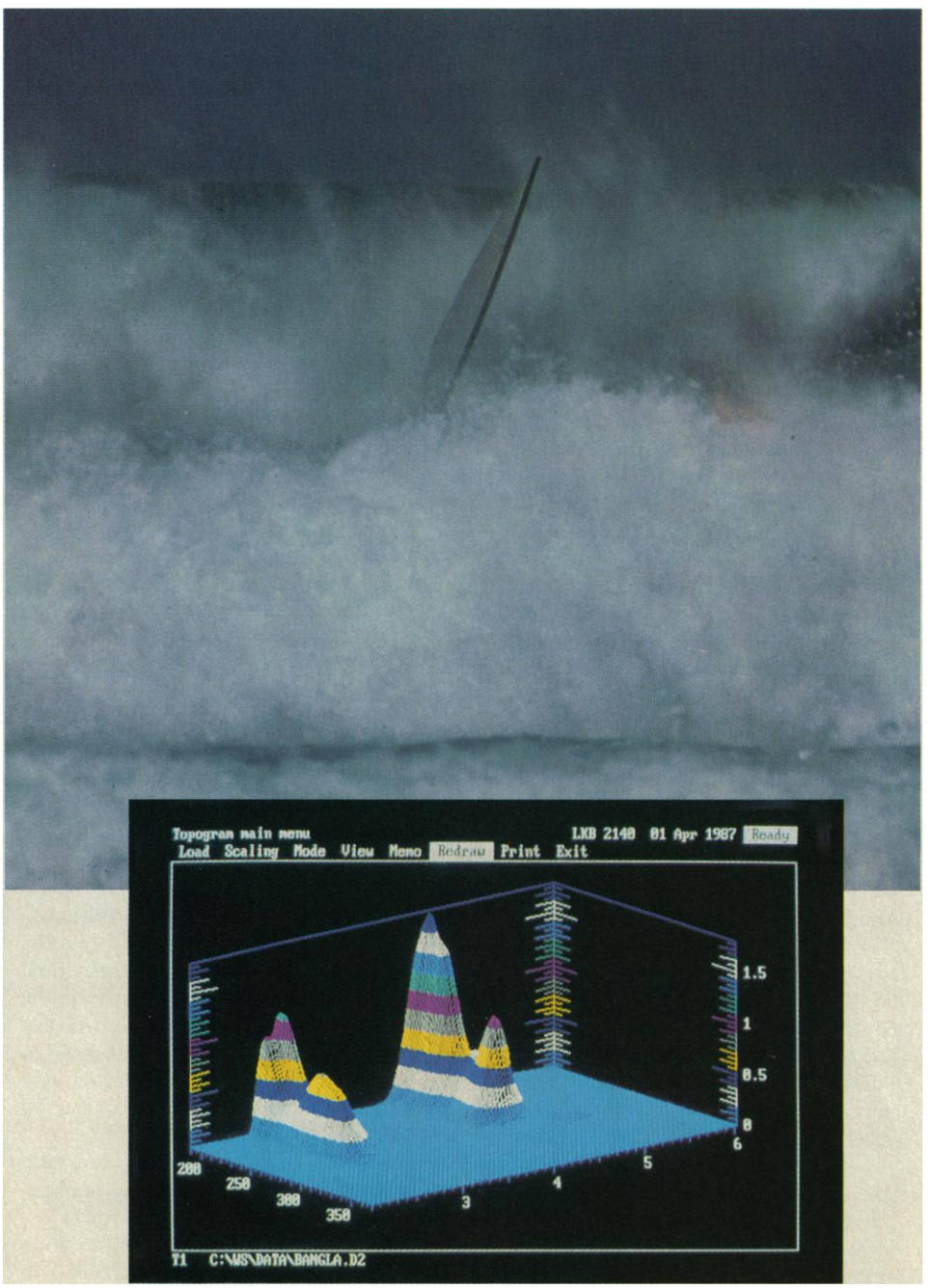

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information about the volume within the pressure boundary, which determines how large a pressure rise would accompany a given release into the containment-confinement volume. U.S. plants have either large dry-volume containments or somewhat smaller volumes supplemented with ice-water systems to condense vapor and thus reduce the pressure increase; they are designed to withstand a complete break of the largest pipe in the system. Chernobyl's RBMK-1000 confinement systems design, on the other hand, has a much smaller volume and is in fact designed to accommodate at most the rupture of only one of the more than 1600 small pipes passing through the graphite stack that constitutes the core.

Ahearne does not compare releases and health effects. The TMI containment performed its design function: virtually no radioactivity (other than noble gases, which contribute little to population exposure) was released, and the offsite health effects were virtually negligible. By now, the severe radiological impacts of Chernobyl are well known. This difference reflects the radical differences in design and safety philosophies that underlie the features of the two reactors and profoundly affected the consequences of the two accidents.

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Response: Silver is correct that the Chernobyl RBMK reactor is far more sensitive than the TMI reactor. However, as I stated in my article (p. 677), the TMI "design is well known within the U.S. nuclear reactor industry as being more responsive to perturbations than other U.S. reactors." Nuclear Regulatory Commission studies after TMI showed that for some accident scenarios involving this type of reactor, operator reaction times would have to be much less than 2 hours.

With regard to the TMI operators' ignorance of the status of the PORV, the operator interpretation was complicated by the operating staff's willingness to allow a violation to go uncorrected. That PORV had been leaking for weeks (*1*, p. 46). Company instructions called for the block valve to have been closed under those conditions (*1*, p. 116). But it had not. This was a violation of required procedures (*2*). Very early in the accident an operator read that temperature downstream of the PORV was 50°F higher than the maximum allowable, indicating the valve was stuck open (*3*, p. 14). Over the next 3 hours, the operators disregarded additional warnings and misinterpreted indications, such as rise in containment pressure (*3*, pp. 17 and 18). However, when the Babcock & Wilcox technical support person was briefed over the phone on what was happening, he immediately figured out that the block valve should be closed, and the replacement shift supervisor took only 20 minutes to reach the same conclusion (*3*, p. 19). The TMI crew did take deliberate actions, even if misguided: "the operators override the emergency system and sharply reduce flow from the HPI [high pressure injection] pumps" (*3*, p. 17). "There is no question that operators erred when they interfered with the automatic operation of the high pressure (HPI) system even though conditions that initiated the system (low pressure) persisted . . ." (*3*, p. 102). It is also true that the operators had not been trained to handle the events that were developing at TMI: "It is a human intervention in the automatic chain of events not inconsistent with the operators' training . . ." (*3*, p. 17). One major review concluded: "First, the operators on duty had not received training adequate to ensure that they would be able to recognize and respond to a serious accident . . . Second, neither the operating crew nor their supervisors . . . possessed the necessary combination of technical competence and familiarity with the plant . . ." (*3*, p. 103). Nevertheless, "these operating personnel made some improper decisions, took some improper actions and failed to take some correct actions, causing what should have been a minor incident to develop into the TMI-2 accident" (*1*, p. 27).

I agree there were major differences in design and safety philosophy. However, complacency, lack of understanding, inadequate training, and poor management were not that different, unfortunately.

JOHN F. AHEARNE
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2. "Investigation into the March 28, 1979 Three Mile Island accident by the Office of Inspection and Enforcement" (NUREG-0600, Nuclear Regulatory Commission, Washington, DC, August 1979), pp. I-1–5.
3. M. Rogovin and G. T. Frampton, Jr., "Three Mile Island: A report to the Commissioners and to the public" (NUREG CR/1250, Nuclear Regulatory Commission, Washington, DC, January 1980), vol. I.

Erratum: In the issues of 21 August (p. 816) and 28 August (p. 956), the volume number (237) was incorrectly given as 238 in the Table of Contents heading.

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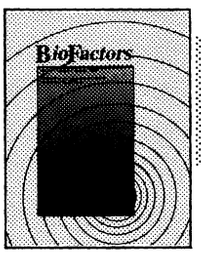

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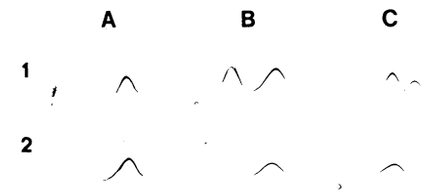

Fig. 4. Crossed immunoelectrophoresis of α_2-AP moieties without (**A** and **B**) or with (**C**) the addition of Lys-plasminogen in the first dimension. (A1) nα_2-AP in plasma; (A2) purified rα-AP-∇Ala; (B1) purified rα_2-AP preincubated with plasmin; (B2) purified rα_2-AP-∇Ala preincubated with plasmin; (C1) nα_2-AP in plasma; and (C2) purified rα_2-AP-∇Ala. Crossed immunoelectrophoresis with rabbit antiserum to α_2-AP with or without the addition of purified Lys-plasminogen (140 μg/ml) was performed as described (*13*). Preincubations of 10 μ*M* rα_2-AP-∇Ala with 5 μ*M* plasmin were for 1 minute at 37°C, after which $2 \times 10^{-4}M$ D-Val-Phe-Lys-CH_2Cl was added.

AP-∇Ala shows no complex formation, in agreement with the SDS-PAGE results. That rα_2-AP-∇Ala maintains the plasminogen-binding function associated with the 26 amino acids at the COOH-terminal of nα_2-AP (*11*) is shown by modified CIE (*13*), in which Lys-plasminogen, a partially degraded form of native Glu-plasminogen, is added to the gel matrix. In this case nα_2-AP in plasma reveals two peaks of plasminogen-binding (slower mobility) and non-plasminogen-binding (faster mobility) material, whereas nearly all of the rα_2-AP-∇Ala, which was purified with LBSI-Sepharose, is in the plasminogen-binding form, as evidenced by its retarded migration (Fig. 4). In CIE, the behavior of rα_2-AP-∇Ala is similar to that of nα_2-AP-∇Ala.

Although rα_2-AP-∇Ala reacts normally with the LBS of plasminogen, it does not inhibit plasmin irreversibly. Whereas under second-order conditions, plasmin is inhibited by nα_2-AP or rα_2-AP with a k_1 of 2×10^7 to $4 \times 10^7 M^{-1}$ sec^{-1} (*8*), no inhibition is observed with rα_2-AP-∇Ala. Even when plasmin is incubated with up to a 20-fold molar excess of rα_2-AP-∇Ala, no irreversible plasmin inhibition is observed.

In conclusion, a three–base pair (GCG) in-frame insertion within the structural gene of α_2-AP has been identified in two true heterozygotes and in their two homozygous children. This alanine insertion, in an area homologous to the 4A β-pleated sheet of cleaved α_1-AT (immediately adjacent to the reactive site), must have resulted in some structural perturbation that has abolished the plasmin inhibitory activity of α_2-AP Enschede and converted the protein to a plasmin substrate. To our knowledge, α_2-AP Enschede constitutes the only instance in which a mutation within the reactive-site region has inactivated a serpin, yet it has converted the inhibitor to a substrate. This naturally occurring mutant may serve as a model for further investigation of the structure-function relationships in α_2-AP, or in serpins in general, that determine the relative properties of an inhibitor as opposed to those of a substrate.

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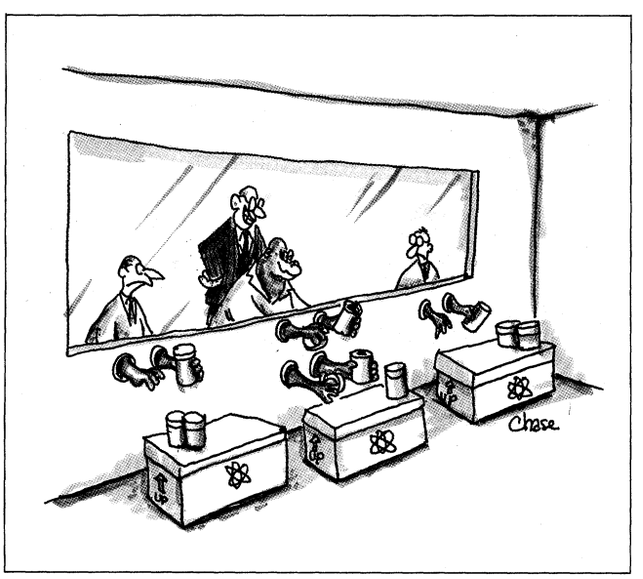

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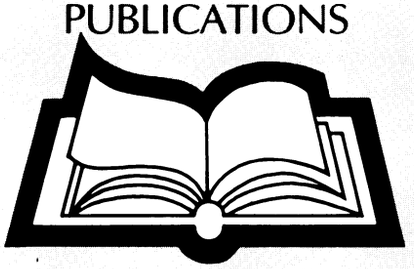

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Oceangoing Animals

Seabirds. Feeding Ecology and Role in Marine Ecosystems. J. P. CROXALL, Ed. Cambridge University Press, New York, 1987. viii, 408 pp., illus. $59.50. From a symposium, Moscow.

Marine ornithology has come a long way in the last 15 years. Oceanographers now think of seabirds as respectable marine animals, instead of casual, terrestrial vagrants. Ornithologists, in turn, have stopped thinking of the sea as a mysterious waste into which their birds disappear from time to time. They are trying instead to fit seabirds into the higher trophic levels of the appropriate marine ecosystems. The present volume gives us a summary of the current state of this art. It stems from a symposium held in 1982 at the XVIII International Ornithological Congress; the presentations have been updated to include material published as recently as 1986.

The 15 papers in the volume are about the relationships between seabirds and their prey, considered from many angles. Four of the papers are straightforward summaries of diet and feeding ecology: in penguins (Croxall and Lishman), procellariiforms (Prince and Morgan), pelecaniforms (Schreiber and Clapp), and Pacific alcids (Vermeer, Sealy, and Sanger). The alcid paper is a useful complement to Nettleship and Birkhead's *The Atlantic Alcidae*. Four more discuss the trophic relationships of seabird communities: in the Gulf of Alaska (Sanger) and off Hawaii (Harrison and Seki), California (Briggs and Chu), and South Georgia (Croxall and Prince). Schneider, Hunt, and Powers model energy flux and make interesting comparisons between the seabird communities in the Bering Sea and on Georges Bank off Massachusetts. Duffy and Siegfried look at food consumption by seabirds in the Humboldt and Benguela currents, the two major Southern Hemisphere eastern boundary upwellings, using guano statistics to obtain a historical perspective. The remaining papers deal with the ways in which seabirds actually find their food: reviews of kleptoparasitism (Furness), diving with particular reference to penguins (Kooyman and Davis), and the complexities of flight itself (Pennycuick). Hunt and Schneider turn the question on its head and discuss the spatial and temporal scales of the "patches" of prey that seabirds must exploit if they are to forage economically. Finally, Croxall considers the general factors that limit seabird populations and the restraints imposed by our own activities as marine polluters and rival fishermen.

I have a few quibbles. One is the limited number of species discussed in most of the papers—auks, penguins, pelecaniforms, and procellariiforms, all cold-water species. This reflects the bias of current seabird research, but it is clear that the restriction is to some extent self-imposed. There is some overlap in subject matter among papers—especially those about the North Pacific—but that is inevitable in a symposium. I did not find the treatment of seabird diets very inspiring—diet papers never are. The contributions on trophic interactions are much more interesting. However, my prize for the best paper in the book goes to Colin Pennycuick's lucid exposition of seabird flight.

John Croxall and his co-authors have pro-