Environmental Variables in Disease

Remarkable correlations have been reported recently between incidence of certain diseases and certain geographic and other environmental variables. Attendants at the AAAS meeting in Montreal, to be held 26–31 December, will have a fine opportunity to learn of these developments. Two symposia have been arranged:

Medical Geology and Geography

A symposium on Medical Geology and Geography will be held Monday, 28 December.

The purpose is to explore the apparent relationship between high incidence of such diseases as cancer and heart disease in certain geographic and geologic areas, and unusually high levels of trace metals in both soil and vegetation.

Among the papers to be given:

—Symposium arranger Harry Warren, University of British Columbia, is not an epidemiologist but a geological engineer.

Warren was led to his current interest in the relationship between disease rates and trace elements in the soil almost accidentally.

He found a useful geological prospecting tool in the fact that the presence in rock strata of certain metals could be detected because the area's vegetation varied from normal in chemical analyses. Trace levels of various metals had been taken up by the vegetation!

Warren will report the remarkable findings of British health officer E. D. Allen-Price: He plotted on a map all deaths during 1939–1958 in an area of west Devonshire, marking cancer deaths with a cross and deaths from other causes with a circle.

Allen-Price reported, "The extraordinary distribution of the disease then became apparent. For example, in one hamlet the ratio of crosses to circles is 1 in 12, whilst in an adjoining hamlet of a comparable community the ratio is 1 in 3."

Warren analyzed rock, soil, and food samples from the area. All vegetables studied "carried anomalously high amounts of lead, never less than 10 parts per million (ppm) in ash, but two samples, one of gooseberries and one of lettuce, from high cancer areas carried 250 and 300 ppm, respectively."

—Helen L. Cannon and D. Ann Fidler of the U.S. Geological Survey, Denver, have studied trace element levels in edible plants and soils in areas markedly different in rates of cancer and heart disease.

Working in areas of New York, Maryland, and New Mexico, they found that plants and soils in areas of high incidence of cancer and heart disease contain more arsenic, nitrate, boron, manganese, chromium, titanium, and lead, and less strontium than do areas with opposite disease patterns.

—Linking the work of the geologists and the biochemists, pharmacognosist Anna Koffler of Ohio Northern University will report on medicinal plants.

Examining 26 medicinal plants, she found a clear relationship between amounts of trace elements in the plants and in the soils in which they grew.

—Metal binding (chelation) may be a mechanism importantly involved in the action of cancer-causing agents (carcinogens) and antitumor agents, suggests chemist Arthur Furst of the University of San Francisco.

Furst notes that practically all drugs found to have anticancer activity either are chelating agents, or easily form chelates themselves.

Other evidence: Cells contain about eight metals which are either associated with enzyme action, or possibly essential to maintain the conformation of nucleic acids. Bodily tissues during the aging process accumulate and concentrate at least 20 other metals, some of them proven carcinogens.

—Members of Britain's College of General Practitioners are being recruited to do field research in epidemiology in their home communitities. The goal is to develop large-sample statistical evidence of relationships between disease patterns and various environmental variables, such as amounts of trace elements in soils and vegetation. A standard classification of diseases has been introduced to facilitate this.

For example, one study region is the valley of the Tamar River, which divides Devon from Cornwall. Here mining has been carried on for centuries. And here Warren drew attention to gross anomalies in the trace mineral content of vegetables grown for human and animal consumption. A group of general practitioners are examining patients and recording morbidity patterns in the area's population of 24,000.

The field research will be reported by R. J. F. H. Pinsent, Birmingham, England, founding member of the College and for 10 years chairman of its research committee.

Geography and cancer death rates. These data were collected by Allen-Price for west Devon, England, for the period 1939–58. Warren found high lead concentrations in vegetables from the high-cancer areas.

Parish	Population	Cancer deaths/1000 living	Percentage of cancer deaths to all deaths
Bere Ferrers	2054	3.2	22.3
Buckland Monachorum	2686	1.8	14.3
Lydford	2071	1.2	16.8
Marystowe	243	1.8	25.0
Sampford	120	6.9	46.7
Sydenham Damerel	235	3.7	22.2

Environment and Oral Disease

In recent years, factors in addition to heredity have been suggested as possible causes of oral disease.

Many of these "candidates" will be examined in a symposium on Environmental Variables in Oral Disease, to be held 26 and 27 December. Arrangers are Frank J. McClure and Seymour J. Kreshover of the National Institute of Dental Research (NIDR), Bethesda.

Among the speakers will be:

—Oral diseases are not quick, dramatic killers. Yet they can cause as much suffering as any disease. In their painful, tenacious way oral diseases are not unlike rheumatoid arthritis, suggests epidemiologist Albert L. Russell of NIDR.

Russell has circled the world to study oral disease incidence and factors which may affect it.

Fluorine in water is certainly a factor, he says. But it is far from the only one—Colorado Springs has a high level of fluorine in its water, yet its citizens have caries incidence far higher than do people in southeast Asia.

Diet appears to be a critical factor, Russell adds. Caries seem to be a disease of "civilization"—Alaskan Eskimos and East Indians alike, when transplanted from their traditional rural

Geography and caries incidence. These data show the range of tooth decay found in a worldwide survey by Russell for civilians of ages 20 to 24. All data were collected during the past 6 years.

Location	Average number of decayed, missing, and filled, permanent teeth
Ethiopia	0.3
Ecuador	8.4
Baltimore whites	13.3
Aleuts in Alaska	17.7

cultures to cities where other cultures predominate, show sharply increased caries levels.

Sugar is one apparent culprit. In Thailand, where 95 percent of caloric intake is from rice, caries incidence is low.

Studies apparently have "cleared" the following as possible culprits: vitamin A, vitamin C, thiamine, riboflavin, niacin, iron, protein, calcium and obesity, Russell reports.

There appear to be unknown factors. Examine the citizens of a South Vietnam village, of any age group, and one finds a factor of two separating high and low levels of periodontal disease. Yet no nutritional difference has been found.

—Trace amounts of other elements than fluorine in food and soil water appear to have a marked effect on caries incidence.

An exhaustive review of studies which support this view will be presented by epidemiologist Capt. Fred L. Losee, USN, of the Great Lakes (Ill.) Naval Training Center.

Losee reviews evidence that ten or more factors may play significant roles. Trace amounts of the following elements all may improve caries resistance: selenium, iodine, vanadium, strontium, molybdenum, phosphorus, boron, and aluminum. Further, some studies suggest that calcium and magnesium are beneficial if present in the ratio of 4 to 1.

—Is the level of tooth decay in an individual due to inherited factors, to a cariogenic flora (for example, streptococcus) in the mouth, to other factors, or to a combination?

Dr. Rachel Larson of NIDR has done a long series of tests with two strains of rats having different levels of caries activity. Her work tends to confirm that both heredity and environment are factors.

But things are not so simple: Crossbred rats caged with the caries-susceptible strain had *caries levels* closer to that of the caries-resistant strain. And they had *caries distribution* around their teeth closer to that of the caries-susceptible strain!

Still unclear are the exact factors, or combinations, causing caries. Dr. Larson suggests four good possibilities: morphological and chemical differences in teeth; differences in quality and quantity of saliva, which may differently affect oral microflora or the clearance of food; one strain of rat may be normally infected with a more cariogenic microflora; or eating, drinking, or coprophagy habits of various strains of rats may differ.

—In 1962 came the story of the tranquilizer Thalidomide and the babies with undeveloped limbs caused by the mothers taking the drug.

Then last year the antihistamine meclizine hydrochloride (Bonine) was shown [*Science* **141**, 353 (1963)] by endocrinologist C. T. G. King of NIDR to cause gross malformations in rat fetuses.

There are contradictory reports that Bonine, which is available commercially without prescription, may cause malformations in humans.

King reports there is no firm evidence either way. Further, it appears that the fault does not lie with a general characteristic of all antihistamines, but only with Bonine and its close relative, chlorcyclizine.

—A key biochemical step in the bodily use of vitamin C was clarified last spring [*Nature* **202**, 302 (1964)] when a specific enzyme was tied to bone formation.

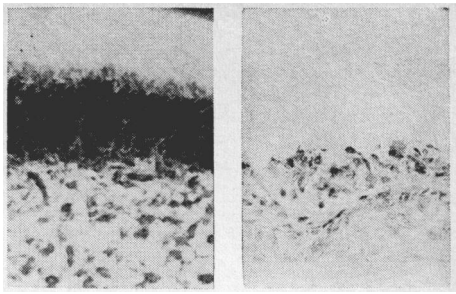
Histochemist Harold M. Fullmer and biochemist George R. Martin, both of NIDR, found that the enzyme beta-hydroxybutyric dehydrogenase is in abnormally short supply in the bone- and dentin-forming cells of scurvy sufferers, although the enzyme is not in short supply in cells that resorb bone.

Although a definite and proportionate relationship exists between the activity of the enzyme and the degree of scurvy in cells producing connective tissue, the precise mechanics of this relationship are undetermined.

It is important to know the specific actions and effects of vitamins in cellular metabolism in order to develop rational therapy.

Fullmer and Martin also have tried to detect a specific enzyme alteration in Paget's disease of bone, but without success to date.

—Dental caries is a multicause disease, and so must be tied to causes by techniques which take this fact into account, suggests Irwin I. Ship, University of Pennsylvania.



Lack of vitamin C has dramatic effect upon tooth development in guinea pigs. Photos show sections near apex of lower molars: Normal tooth (left) shows dark band indicating high level of enzyme activity just below dentin band at top. Black band is absent in scorbutic tooth.

Ship examined American Indians in North and South Dakota and found an apparent relationship between caries incidence in them and the presence of a phosphate additive in the bread they ate. Those eating the phosphate bread appeared to have fewer cavities.

To double-check the relationship, Ship subjected the available data to multifactor analysis. He found that the cause of the varying caries incidence in the Indians was not the phosphate but population changes, inadequate matching of groups, and changing age-sex distribution of the subjects.

Ship concludes that some current beliefs as to the causes of caries may be unsupported and should be re-examined with new statistics-computer tools. He reports that the techniques are surprisingly easy to master.

Date Changes

The November issue of the *AAAS Bulletin* is devoted entirely to reports on the Montreal meeting. Several of these were incorrectly dated. The correct dates are:

Mathematics—Films with Commentary, 29 Dec.

Psychology—Activation, 30 Dec.

Social and Economic Sciences—Research Environment, 28 Dec.; Training Programs, 28 Dec.

Dentistry—Environmental Variables in Oral Disease, 26–27 Dec.

Information and Communication—Vice-Presidential Address of Wallace Brode, 30 Dec.

Academy Conference, 27–28 Dec.

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