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The influence of soil on infectious disease

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'... the regions in the Aveyron, where we find anthrax, have a calcareous clay soil, and the parts where anthrax is unknown have a schistose or granite soil.' (L. Pasteur[37])

As has been true for so many other aspects of microbiology, the early seminal observations on the roles of soil in infection were made a century ago by Pasteur. He demonstrated the capacity of earthworms to transport cylinders of earth from the depths to the surface. Thus, he proposed that the soil surface could become contaminated with pathogens from dead, decaying host tissues that had been deeply buried. Pasteur considered that one reason for the lack of anthrax in granitic soil might be the relative difficulty of earthworm survival in such terrain. We will suggest below an alternative theory for the uneven distribution of anthrax. Indeed, a considerable variety of mechanisms can be envisioned whereby soil could modulate the incidence and severity of specific infectious diseases. Possible mechanisms are listed in the table.

Suppression or strengthening of host defense by soil minerals

To test the likelihood of mechanism No. 1 in the table, 5 mg of sterilized soil was combined with 100 cells of *Staphylococcus aureus* in wound incisions in guinea pigs[41]. In the absence of soil, no infections ensued; with soil, infection developed in > 80% of the test animals.
Infection-potentiating factors were present in soils of either high or low organic content. In the latter, sand and silt were much less active than clay. Of the clay minerals, montmorillonite was more active than illite or kaolinite. Infection potentiation was correlated with cation exchange capacity. Thus, the authors proposed that organic components or montmorillonite, each strong in this attribute, can force detrimental amounts of cations into host defense fluids and tissues.
In a subsequent study with *S. aureus* and *Pseudomonas aeruginosa* in the same laboratory, 10 mg of sterilized montmorillonite particles, less than 2 μm in diameter, were reported to eliminate the anti-bacterial activity of 1 ml of serum as well as markedly impair the phagocytic and bactericidal ability of 25,000 leukocytes[21]. Unfortunately the investigators failed to determine which specific cation(s), if any, were being altered in availability by the clay mineral. Of the physiologically active metallic ions, only ferric iron consistently suppresses serum and leukocytic antimicrobial activities[68]; however, metallic ions, such as those of aluminium, that are considered physiologically inert have not been adequately studied. Future investigations might examine possible mobilization of aluminum from the clay silicates to suppress host defense, as well as possible ability of the silicates to increase the level of iron contamination in soil-infected wounds.
On the other hand, specific components of soils, if assimilated into the tissues via ingestion of plant or animal food or drinking water, could possibly strengthen host defenses against infection (item No. 2, table). The most obvious and well-studied example is that of the ability of soil mineral elements to improve resistance of tooth enamel to the acids formed by cells of *Streptococcus mutans*. In many reports on dental caries, prevalence is inversely correlated with fluoride ion levels in drinking water. However, when fluoride content of rock, soil, and water is low, effects of other minerals are sometimes noted. For example, caries prevalence of 1876 12–14-year-old lifelong residents of 19 communities with populations of 3000–15,000 in the eastern United States was examined[59]. The communities were situated on four different soil types and each used water containing < 15.7 μM F. Caries incidence was highest on the podzol soils of New England, lower on gray-brown and red-yellow podzols, and lowest on the subhumic gray soils of the South Atlantic states.
In New Zealand, the adjacent cities of Napier and Hastings have significantly different caries prevalence rates despite similar dietary habits, socioeconomic conditions, and fluoride content of drinking water. Vegetables grown in the Napier soil generally were found to be richer in molybdenum, aluminum, and titanium and poorer in copper, manganese, barium, and strontium, as compared with those grown in the Hastings soil[59]. The higher molybdenum content of the Napier vegetables was proposed as a factor in the lower prevalence of caries in the children of that city.
Other examples of the ability of soil minerals to strengthen host defense include enhancement of the microbicidal action of rodent and bovine neutrophiles by selenium[7] and of ovine and bovine macrophages by cop-

per[24]. Note that 'there is a tendency for the amounts of trace elements in soils to parallel those in the rocks from which they are derived, and for vegetal matter to reflect the composition of the soils on which it is growing.... the trace element content of rocks, soils, and foods varies far more than is generally realized by most medical men, geographers, and epidemiologists'.[65]

Selective inhibition of pathogens by natural products in soil

During the past four decades, approximately 5500 antibiotics have been characterized; 150 of these are produced in industry for agricultural, veterinary, or medical purposes[13]. The capacity to synthesize antibiotics is common among soil saprophytes and has been observed in unsterilized soil[13]. The quantities of available transition series metal ions as well as phosphate are very critical in the derepression of synthesis of antibiotics and other secondary metabolites[67]. Based on laboratory observations, significant yields of secondary metabolites in soil would be predicted to require not only appropriate amounts of carbon and nitrogen, but a very low quantity of phosphate and fairly precise concentrations of zinc (for fungi), of zinc and iron (for actinomycetes), of manganese (for *Bacillus* sp.), and of iron (for other bacteria)[67]. Such yields of antibiotics might then be sufficient to prevent growth of bacterial or fungal pathogens in the soil, provided that the compounds were not rapidly destroyed by other microorganisms.

Although evidence is not presently available that antibiotics in soil actually suppress microbial pathogens, an example that does illustrate item No. 3, table, is that of siderophore production. In soils of low iron availability, siderophores are formed by some microbial species in amounts that can suppress growth of plant pathogens. Specific strains of soil pseudomonads form hydroxamates (e.g., pseudobactin) that prevent growth, by means of iron deprivation, of such plant pathogens as *Erwinia, Fusarium,* and *Gaeumannomyces*[28]. Fortunately the hydroxamates do not interfere with the ability of the plants to acquire iron; on the contrary, soil siderophores are considered to be of great importance in facilitating iron uptake in plants[11].

Soil pH and mineral availability might selectively suppress saprophytes to permit growth of pathogens

An increasing number and variety of microbial pathogens are being recognized to be able to survive and, in some cases, to multiply in well-defined soil domains termed 'incubator areas'. Notably, as it had in the era of Koch and Pasteur, *Bacillus anthracis* has served as the initial model. In the 1950s, Van Ness recognized that vegetative cells and spores of the anthrax agent are eliminated in acid soils, possibly because of biological competition[62]. He observed that incubator areas for *B. anthracis* may form in: 1) depressions in which water has remained sufficiently long to devitalize or kill grass, 2) desiccated ephemeral watercourses, or 3) hillside seep areas. Multiplication of the vegetative cells of *B. anthracis* is favored by either calcareous soils or alkaline groundwater and is suppressed in fields over shale or sandstone or in those that are well drained. These pioneering observations of

Some possible mechanisms whereby soil might alter the incidence and intensity of specific infectious diseases

Item	Reference
1. Soil minerals might suppress host defense factors	21, 41, 3
2. Soil minerals might strengthen host defense factors	7, 24, 59
3. Soil natural products might selectively suppress growth of pathogens	28
4. Soil pH and mineral availability might selectively suppress growth of saprophytes and permit growth of pathogens	This paper
5. Soil aridity and temperature might selectively favor or suppress survival and growth of pathogens	1, 6, 8, 12, 17, 22, 36, 38, 39, 54, 69
6. Soil might affect survival and growth of intermediate hosts or vectors	3, 5, 18, 20, 23, 32, 33, 44
7. Soil foci that contain pathogens might become airborne	4, 9, 10, 14, 19, 30, 47, 49, 51, 56, 57, 64

Van Ness on soils in the Western Hemisphere now have been extended and confirmed for soils in the Eastern Hemisphere[26].

Soil pH profoundly influences availability of mineral elements, including physiologically important trace metals[23]. Of the latter, manganese concentrations are especially critical for species of *Bacillus*. Consistently, at least 100 times more of this metal than the quantity of 0.1 μM needed for vegetative growth is required by cells of this genus for derepression of synthesis of such secondary metabolites as antibiotics and exotoxins, and of such entities as bacterial viruses and endospores[66]. Although arable soils generally vary in manganese concentration from 200 to as much as 10,000 μM, in many soils the metal becomes unavailable to plants at pH levels above 6.25–6.5 because of the formation of insoluble manganese dioxide[46]. Deficiency of available manganese is common on calcareous peats, on other soils having a high content of organic matter, on limed soils, and on soils with a high water table[46].

Of the various species of *Bacillus,* that of *B. anthracis* could be predicted to thrive much better than saprophytic species at suboptimal levels of manganese. Recall that *B. anthracis* uniquely produces an exotoxin; this secondary metabolite consists of three chemical components of which factor I, not toxic itself, is a very powerful chelating agent[50]. Conceivably, factor I acts as a manganophore in alkaline environments to secure a sufficient quantity of the metal for synthesis of factors II and III, as well as for sporulation of *B. anthracis*. Presumably, other species of *Bacillus* apparently can neither form the chelator nor use molecules of factor I synthesized by *B. anthracis* and thus cannot compete with the latter for occupancy in the alkaline niche.

Additional pathogens observed to thrive in neutral-to-alkaline soils include *Clostridium novyi* (the agent of bacillary hemoglobinuria)[63], some but not all types of *Cl. botulinum*[23,58], *Erysipelothrix rhusiopathiae* (the agent of swine eryslipelas)[23], and *Leptospira* spp. (the agent of leptospirosis)[23]. Survival of these pathogens is more likely to be dependent on availability of iron rather than manganese; as with the latter metal, acquisition of iron is quite difficult at alkaline pH values. Again, it can be proposed that the alkaline environment would selectively suppress saprophytic relatives of the pathogens by interference with iron uptake[68].

As a corollary, pathogens that cannot synthesize siderophores but which are dependent on those made by other strains would be predicted to occur more commonly in acidic than in alkaline environments. An example of such a pathogen is *Mycobacterium paratuberculosis*, the agent of Johne's disease[48]. This disease occurs in cattle raised on acid but not on alkaline soils[29]. Likewise, pathogens that require unusually high amounts of iron-presumably because of impaired acquisition systems – such as *Listeria monocytogenes*[55], would be expected to prefer acid soils for growth and this is indeed the case[60]. Type C strains of *Cl. botulinum* also occur in acid soils[23]; however, competence of these strains to acquire iron has not yet been studied. Some pathogens (e.g., *Histoplasma capsulatum*)[43], prefer soils at or close to pH 7.0.

Soil aridity and temperature might selectively favor or suppress survival and growth of pathogens

A few examples are available in which hot, arid soil permits pathogens to survive and grow while suppressing saprophytes. For instance, under hot, dry geocarposphere conditions, *Aspergillus flavus* (the agent of aflatoxicosis) is able to multiply when growth of *A. niger* and other associated saprophytes has ceased[22]. When the soil moisture approaches the minimum for growth of *A. flavus*, such growth is possible only with temperatures at or close to 35°C. In contrast, in hot but moist soil, *A. niger* grows vigorously and either inhibits aflatoxin formation by *A. flavus* or degrades any aflatoxin that is produced[22].

Another example of a pathogen that grows in soil in which competitive saphrophytes have been suppressed by aridity and high temperature is *Coccidioides immitis*, the agent of coccidioidomycosis[12]. This fungus grows in light, slightly alkaline, uncultivated soil that has sparse vegetation, annual rainfall of 15–30 cm, and hot summer temperatures that markedly reduce the microbial population in the upper 10–15 cm. At mid-day the soil surface temperature can attain 65–75°C. *C. immitis* can survive below the hostile surface at depths as great as 20 cm[1]. After the rainy season and in periods of less intense heat, the surface is reinvaded by *C. immitis* and it sporulates heavily. With the return of adverse conditions, winds disseminate the infectious spores before the heat and dryness kill the surface growth[1]. In the Western Hemisphere, these soil conditions and the fungus are found in the Lower Sonoran Life Zone in areas of California, Arizona, Nevada, Utah, New Mexico, and lower California. The pathogen occurs also under similar conditions in small areas of Central America and in the Grand Chacos-Pampa region of South America[12].

On the other hand, the literature contains a considerable variety of examples of pathogens whose survival or growth are suppressed by lack of soil moisture. Among bacteria, for instance, *Pseudomonas pseudomallei* (the agent of melioidosis) was identified in 15–33% of samples from wet rice fields or newly planted oil palm but in only 1–3% of drier, forested soils[54]. Similarly, *Yersinia enterocolitica* (an agent of enterocolitis) was isolated from soils only on days for which rainfall in excess of 17 mm had occurred during the previous week[6]. Likewise, long periods of sunshine with few of rainfall reduced the survival of *Salmonella typhimurium* in cultivated soils[39]. Among protozoan pathogens, cysts of *Entamoeba histolytica* (the agent of amoebic dysentery) were found in 14–52% of Gambian natives in the dry season but in nearly 100% as the rains commenced[8]. Similarly, in Somalia, a lower incidence of infection with *Toxoplasma gondii* occurred in persons living in arid zones as compared with those residing in humid soil zones[69]. The cysts of *T. gondii* are known to survive longer in humid than in arid soil zones[69].

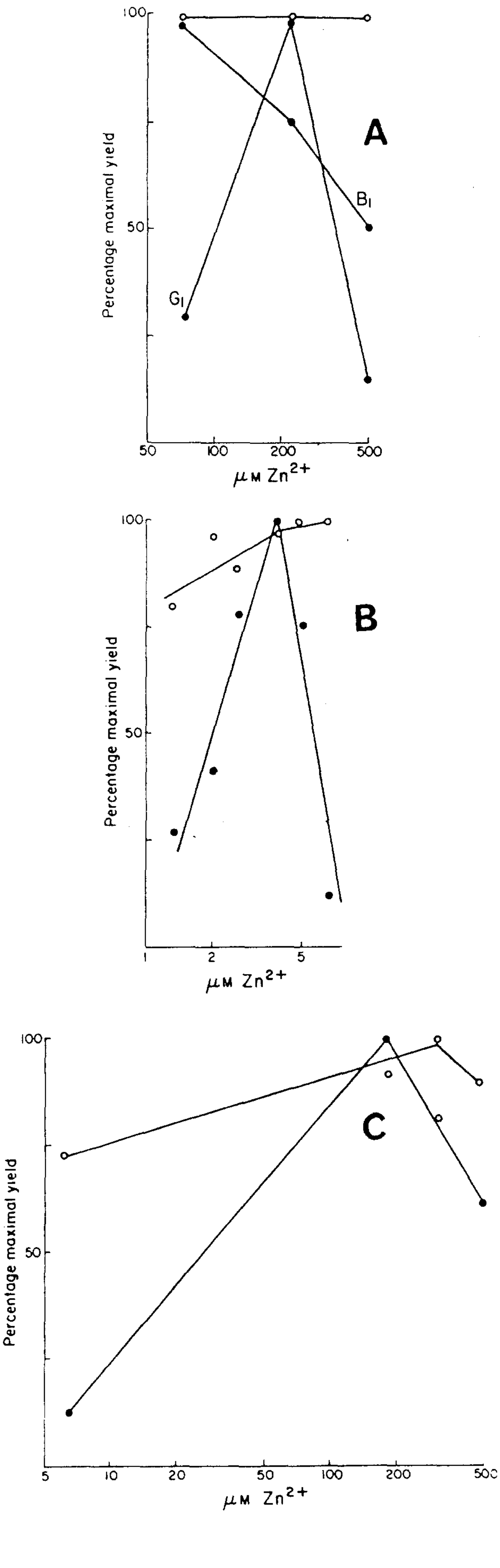
Among helminthic pathogens, survival of eggs of *Toxocara* spp. (the agents of canine and feline roundworm infestations) is enhanced in moisture-retaining clay soils[17]. The eggs are concentrated by the spreading and sorting action of rain and are sedimented in a layer of fine silt between a thin protective blanket of colloidal clay and a deeper layer of coarser particles. Thus, the eggs settle out of suspension well below the surface, where they are protected from sunlight and drying. Although larval development ceases at $< 10\,^{\circ}C$ and death occurs at $< -15\,^{\circ}C$, eggs survive and retain infectivity through relatively mild winters as far north as Québec if the soil surface is protected by snowpack[17].

Of the various ecologic elements that regulate the population of eggs of *Ascaris lumbricoides* (the agent of human ascariasis) outside the host, the most important are soil temperature and moisture[38]. Since the eggshell is permeable to water, desiccation and high temperatures readily kill the eggs. The latter can survive for more than six years in temperate soils but for only a few hours in tropical soils. Similarly, trematode eggs (e.g. the agent of fascioliasis in sheep) are susceptible to desiccation and die if the surface film of moisture is lost. Moreover, the larva must develop in an aquatic snail in habitats that are not completely aquatic. In fascioliasis, habitats are found on pastures that are badly drained and not excessively acid. In England, Wales, and Ireland, records maintained since 1737 indicate that epizootics occurred in every year that followed a wet summer, and especially if the rainfall in June exceeded twice the long-term average for that month[36].

Soil might affect survival and growth of intermediate hosts or vectors

A variety of pathogens of animals and humans spend a portion of their life cycle in intermediate hosts or vectors such as snails, mites, earthworms, or dung beetles. Accordingly, factors in soil, such as minerals or moisture, that affect survival of these creatures should influence morbidity of the specific infectious diseases. For example, proliferation of snails that are required for development of trematode larvae is favored by calcium because the element is needed for shell formation; perhaps, also, calcium might counteract the toxicity toward snails of copper[23]. In contrast, addition of calcium salts to soil was observed to lower the quantity of mites that transmit bovine cestode larvae[3].

Eggs of bovine cestodes have been found in the digestive tracts of dung beetles[33] as well as earthworms[32]. Likewise, eggs of various nematodes of animals and humans can be concentrated and transported by these invertebrates as well as by birds or moles that ingest the contaminated



beetles and worms[5,18,42]. In addition to helminthic pathogens, protozoa also can be transported by earthworms. The latter can serve as vehicles for infection of birds with *Toxoplasma gondii*[44]. Prevalence of pathogenic procaryotes that have invertebrate vectors can also be influenced by soil. For instance, the favored ecotype of the chigger (and its rat host) that transmits *Rickettsia tsutsugamushi* in Indonesia is that of coarse, low-lying native vegetation on a porous coralline soil[20].

Soil foci that contain pathogens might become airborne

Contaminated soil can enter the vertebrate host in several ways: via wounds, ingestion, or inhalation. The latter route is mainly of concern in regard to fungi and bacteria rather than worms and protozoa. Recently, however, soil amoebae were recovered from air during a Nigerian harmattan. The protozoa included pathogenic strains of *Hartmanella* and *Naegleria* which can cause meningoencephalitis in humans[30]. Nevertheless, most research on airborne soil pathogens has been conducted with fungi – notably *Histoplasma capsulatum,* the agent of histoplasmosis.

This fungus has been found in soil throughout the world; in the U.S. it has thus far been identified in 31 of the 50 states[14]. Soils enriched with bat and bird guanos favor the growth of *H. capsulatum* and give it competitive advantage over other soil fungi[1]. Soil foci of *H. capsulatum* are often found in protected areas such as caves, abandoned buildings, chicken coops, or canebrakes that have been heavily seeded with guano of bats, blackbirds, starlings, or grackles. Not all such sites will actually harbor the fungus. For example, in a set of 17 blackbird roosts located in five states in the Mississippi and Missouri river valleys, nine were positive for the fungus, eight were negative[64]. The positive sites contained an average of three times as much nitrogen and twice the amount of organic matter and of phosphorous as did the negative sites.

Disruption of positive soil foci by such human activities as spelunking, clearing[51], or excavating[47], or by tornadoes has resulted frequently in miniepidemics of histoplasmosis. Even such mild activities as gardening or children playing in a contaminated area can result in acute infections[9]. Moreover, outbreaks of symptomatic disease even have been triggered by apparently undisturbed foci of *H. capsulatum*[10,19].

When it has been determined that a positive soil focus is to be disturbed by excavation and subsequent construction, the site can first be decontaminated by application of 3% formalin in a volume of 42 l/m^2 of soil[4]. Safety precautions must be taken so that inhalation by the decontamination team of dust and formalin will be minimized.

A few reports are available concerning soil foci of bacterial pathogens that might become airborne. For example, *Mycobacterium xenopi* was isolated from the sputum of 21 patients with clinical signs of pulmonary disease and

Effect of zinc on yield of mycotoxins. Dry weight of mycelia, ○---○; mycotoxin, ●---●. *1A* alfatoxins (drawn from data in table 1A of reference 35); *1B* fusaric acid (redrawn from figure 1 of reference 25); *1C* rubratoxin (drawn from data in table 6 of reference 15).

of 52 asymptomatic subjects living in the environment of a sludge pool. The bacterium was cultured in high numbers from sludge samples. The infections were assumed to occur partly via dry sludge particles scattered by the wind in summer and partly by sludge used as fertilizer[56].
Likewise, inhalation of soil particles from disturbed excavations is considered to be a source of some, but not all, outbreaks of pneumonia due to *Legionella pneumophila*[49,57]. In one well-documented miniepidemic, for instance, a water sprinkling system was being installed on the 350-acre grounds of a 6000-bed psychiatric hospital[57]. Piles of soil were aerosolized by a 'dusty' storm with a wind velocity of 47 mph. During the subsequent 4–11 days the attack rate of cases in hospital residents located within 20 feet of excavation sites was 52 cases per 2928 persons; for residents distant from such sites the attack rate was five cases per 2858 persons ($p < 0.0001$).

Miscellaneous associations between soils and infectious diseases

Associations between soil constituents and neurological syndromes caused by 'slow' viruses continue to be documented, but it is not yet known if or how the constituents might contribute to morbidity of the disease. For example, soil samples from British and Canadian areas with clusters of cases of multiple sclerosis were found to have four times as much zinc, six times as much copper, and 24 times as much lead as did soil samples from areas without clusters[65]. In Australia, high-risk areas of multiple sclerosis were observed to be associated with acid podzols in which molybdenum was fixed and copper was leached[31]. On the southern coastal plain of west New Guinea, a soil deficiency of calcium and magnesium was associated with a high incidence of amyotropic lateral sclerosis and parkinsonism-dementia[16].
Among other miscellaneous associations between soils and potential pathogens is an observation that, in Ontario, leptospirosis occurs in areas underlain by Paleozoic but not by Precambrian bedrock. The distribution of calcium carbonate is more uniform in Paleozoic rock and the amounts of zinc, copper, and lead are higher in soils overlying such rock than is the case in Precambrian areas. Saprophytic strains of leptospires occur widely in both types of bedrock areas[27].
Noted earlier is the consistently made laboratory observation that the level of environmental zinc regulates expression of fungal secondary metabolism which includes the synthesis of mycotoxins. Illustrations of this generalization are contained in figure 1[15,25,35]. At least one field example has been reported; namely, the amount of zinc in the soil in some areas of Madras permitted formation of the fusarium wilt toxin whereas in other soil areas the zinc content allowed growth but not toxigenesis[45]. Although the soils were similar in other respects, the cotton crop was poor in the first area and good in the second. Note in figure 1B the narrowness of the range of zinc concentration that permitted efficient toxigenesis.
A variety of fragmentary observations on survival and spread of fungi in clay soils are contained in the literature. For example, in soils containing montmorillonite but not kaolinite, *A. niger* was suppressed by *Serratia marcescens*[42]. The bacterial cells had more antifungal activity at pH 5.5 than at 4.8. In another study, montmorillonite but not kaolinite protected fungi in soil from cadmium[2]. However, in the absence of cadmium, montmorillonite suppressed the spread in soil of fusarium wilt fungus[52] and of *H. capsulatum*[53]. The impact, if any, of these associations on disease morbidity is not known.
In some cases, clinical entities that originally were considered to be infections and which are associated with specific soil areas or soil components are found, upon closer scrutiny, to be non-microbial in origin. An example is that of lower leg elephantiasis in inhabitants of areas of red clay soils around volcanos in the Rift Valley and in the Cameroon highlands of Africa[40]. At first the peripheral lymphatic vessels were thought to be congested with filarial larvae; it is now recognized that the blockage is due to silicosis[40].

Conclusions

A variety of mechanisms have been postulated whereby soil characteristics and components might be able to alter the incidence and intensity of specific infectious diseases. Much work, however, remains to be done to precisely ascertain the roles of soil on infection. Indeed, Van Ness has proposed that 'a special field of study embracing the relationship of agricultural practices, soils, and infectious diseases may be necessary to reduce the problems associated with geophytic infectious diseases'[61]. He noted further that 'when the laboratory approach considers only the host and the parasite, it misses the factors that identify infectious diseases with some environments and not with others'.[62]

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The epidemiology of dental caries in relation to environmental trace elements

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Summary. This paper reviews the influence of the geochemical environment on the epidemiology of human dental caries. The best documented association is that between water borne fluoride and reduced caries prevalence. The influence of fluoride was first reported during the early decades of this century in Colorado, USA, and led to the fluoridation of some public water supplies in several countries. In all cases, fluoridation has been followed by significant improvements in dental health and no adverse effects in general health. Other trace elements in food and water have now been linked with dental caries. Molybdenum has been associated with reduced caries prevalence whereas selenium and lead appear to have adverse effects. Cavity formation in teeth probably involves a localised dissolution of the enamel surface by the products of bacterial activity. It is possible that the incorporation of trace metals into the apatite microcrystals of enamel may alter their physical properties, especially solubility, and hence their susceptibility to degradation.
Key words. Apatite; caries; enamel; fluorine; lead; molybdenum; selenium; trace metals; vegetables; water.

Introduction

It has long been believed that 'airs, waters and places' have a direct bearing on human health and environmental influences have been proposed to explain the localised prevalence of some non-infectious diseases[52]. Particular attention has been paid to the geochemical environment since many trace elements are either essential to mammalian metabolism or may interfere with metabolic functions[48, 57] and the trace inorganic composition of water can be influenced by the nature of bedrock and the composition of vegetables reflects that of the soil[56]. Unfortunately, to establish a link between environmental geochemistry and human health is not easy. Indeed, the mobility of people and their obtainment of food and drink from many different, often non-local sources justifies the apparently convincing conclusion that the local geochemical environment must have little influence on health.
Dental epidemiology, however, provides some of the most convincing evidence that trace elements can affect the health of communities.
A dental disease which lends itself for the purpose of the study is dental caries. It is epidemic in many countries and a large population is therefore always available for study. Diagnosis of the disease is through a visual inspection which maximises the willingness of individuals to assist in surveys. Where the survey population comprises children, typically 12-year olds, the time interval between cause and effect is short and it is possible to make direct associations between environmental quality and disease prevalence. In the case of fluoride, a direct link was established over 50 years ago[3, 20] and led to the successful fluoridation of public water supplies.

Caries and Enamel

The outer layer of the crown of a tooth is enamel, the hardest tissue in the body. Beneath it lies the dentine, the main tooth component, in the centre of which is the pulp containing the blood vessels and nerves. Cementum covers the root surface of the dentine and it attaches the periodental ligament to the tooth which in turn holds the tooth to the jaw.
Dental caries is the localised destruction of these tissues commencing with the enamel. The process of this destruction is not fully understood but it is thought to be due to the presence of micro-organisms on the enamel surface. They are responsible for the formation of plaque, in which the bacteria grow and proliferate. The presence of carbohydrate considerably increases the rate of proliferation as it is a substrate favoured by the organisms. As the substrates are metabolised, within the plaque, organic acids are produced which are held, by the plaque, against the enamel until they diffuse away. The initial phase of tooth destruction is most probably due to the dissolution of the mineral phase of the enamel by these acids[19].
The principal component of enamel is microcrystalline hydroxyapatite set in a protein matrix. The protein represents about 1% of the enamel dry weight and appears to resemble keratin except it contains less sulphur. The apatite fraction approximates to the composition
$(Ca_{9.5}Mg_{0.2}Na_{0.1}H_{0.5})\,(PO_4)_{5.7}(CO_3)_{0.5}(OH)_2$
But apatite, whether biogenic or geochemical, contains traces of many other elements which occur in the crystal structure through isomorphous replacement. That is, one ion can substitute for the normal ion if its size is similar and it does not differ in charge by more than one. Many