

Review Article

Environmental Pathology in the Tropics: Diseases of Uncertain Etiology and Environmental Diseases (Part I)

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Some endemic diseases in the tropics suggest that environmental factors, ethnical predisposing factors, and human ecological factors exert an influence upon disease manifestations. This paper is a preliminary trial of a new geopathological approach to diseases of uncertain etiology, and to environmental diseases in the tropics.

Familial Mediterranean Fever and Related Conditions:

Also called benign paroxysmal peritonitis, periodic peritonitis, periodic arthrosis, familial recurrent polyserositis, and periodic or recurrent polyserositis. The disease is characterized by severe recurrent attacks of fever with acute abdominal pain (Siegal, 1945; Andrade, 1952; Sohar *et al.*, 1967). Pain in the chest or joints and erythema resembling erysipelas are occasionally seen. It is sometimes complicated by certain forms of primary amyloidosis on a genetic basis, in which the deposits of fibrillar protein are of the AA type. In some cases, the attack resulted in the formation of residual fibrous adhesions which later occasionally caused further intra-abdominal complications. The disease occurs in certain families and is thought to be transmitted by a single recessive autosomal gene. Clear cut geographical distribution of familial Mediterranean fever and amyloid peripheral neuropathy in the Portuguese have been recognized. It is a hereditary disease usually occurring in Armenians and Sephardic Jews. It very rarely affects Arabs and Maltese. Most of the affected Sephardic Jews had formerly been resident in the North African littoral or in Iraq, and it does not affect Jews of Yemeni or Persian origin.

These facts suggest that familial Mediterranean fever is an endemic disease and manifestations of the disease are influenced by ethnical predisposing factors and ecological factors.

Tropical Ulcer:

Also called tropical phagedenic ulcer, *ulcus tropicum*, tropical phagedena, tropical sloughing phagedena, Aden ulcer, Malabar ulcer, Cochin sore, and Naga (Nagana) sore. Various native names but only geographical significance have been given to the tropical ulcer (Basset, 1969; O'Brien, 1976). The tropical ulcer is a chronic, often progressive, sloughing ulcer, usually occurring on the lower extremities. The pathologic change in the ulcer is essentially a necrosis of the skin and subcutaneous tissues. It may extend deeply, with destruction

of underlying muscles, tendons, periosteum and bone. Squamous cell carcinoma may arise as a rare complication. It is necessary to take into account in the differential diagnosis of other various chronic ulcerations of tropical countries: framboesia (yaws), tuberculosis, leishmaniasis, histoplasmosis, and Buruli ulcer caused by *Mycobacterium ulcerance*. The correct diagnosis depends upon early recognition of the characteristic features in the histopathological picture. The etiology is unknown but spirochetes, fusiform bacilli, and other bacteria are often present in the affected lesion. Protein and vitamin deficiency with lowered resistance to infection may be important in the etiology. It is widespread throughout the tropical areas and is particularly prevalent in malnourished children in the wet tropics.

Ainhum:

Also called dactylolysis spontanea ("to saw" in African). Ainhum is a condition marked by linear constriction of one or both of the little toes and may ultimately result in pathological amputations. A linear constriction around the affected digit leads to spontaneous amputation of the distal part of the digit. Very rarely the 5th finger, index finger or thumb may be affected (Findlay, 1951). The condition was reviewed by Browne (1961). It is practically confined to the darker skinned people in tropical countries, mainly in Africa, North and South America and the West Indies, though it has also been reported occasionally among non-negro races in India and Polynesia. It occurs more frequently in males and chiefly in adult life. It is rare to see the condition in persons who habitually wear shoes. Life style seems a more important to consideration in the pathogenesis. Other examples of disease of dactylolysis spontanea are also seen in leprosy.

Tropical Eosinophilia:

Also called tropical pulmonary eosinophilia, pseudotuberculosis of the lung with massive eosinophilia, eosinophilic lung, pulmonary eosinophilia, benign eosinophilic leukemia, eosinophilia with pulmonary disease, tropical eosinophilic asthma, Frimodt-Möller and Barton disease, and Weingarten's disease or syndrome. The condition is characterized clinically by leukocytosis with an absolute increase in eosinophils, by spasmodic bronchitis with coughing, anorexia and malaise. Routine blood counts of patients show high eosinophilia varying from 20 to 90%. It is characterized by diffuse eosinophilic infiltrations of the lung, and episodic nocturnal wheezing and coughing. The etiology is possibly a subacute or chronic form of occult filariasis, usually involving *Brugia malayi* or *Wuchereria bancrofti*, occurring in the tropics (Webb *et al.*, 1960; Donohugh, 1963; Pacheco and Danaraj, 1963; Neva and Ottensen, 1978; Ottensen *et al.*, 1979). Microfilariae are seldom detected in peripheral blood films since the parasites are confined primarily to the lungs. Tropical eosinophilia is a disease occurring in certain parts of India, Sri Lanka, certain parts of Africa, China, the Philippines, Samoa, West and East Malaysia, the West Indies, and a few other areas. In India, it affects chiefly Asiatic Indians, in whom it may represent a genetic predisposition.

Idiopathic Elephantiasis:

Also called non-filarial elephantiasis (Oomen, 1969a, b; Price, 1972) and lymphostatic verrucosis (Clark, 1948). Elephantiasis is a chronic disease characterized by inflammation and obstruction of the lymphatics followed by remarkable fibrosis of the skin and subcutaneous

tissues. Verrucosis is a condition marked by the presence of multiple warts, or verrucae which are lobulated hyperplastic epidermal lesions with a horny surface. The foot is principally affected, with enlargement, thickening, discoloration, and fissuring of the skin, and occasionally a formation of ulcers. Lymphoedema of the foot or leg is a common occurrence in many parts of the tropics. The term 'mossy foot' is often used to describe the late results of lymphoedema which are characterized by hyperkeratosis of the overlying epithelium giving rise to a mossy appearance. Idiopathic elephantiasis is a disease without any obvious etiology. However, such a picture is seen in the lymphoedema of filariasis, in mycetoma, and occasionally in Kaposi's sarcoma.

Desert Sore:

Synonyms are veld sore, Barcoo rot, Gallipoli sore, and Umballa sore. Also called by various native names and by names having only geographical significance (O'Brien, 1972). This is a form of ulcer resembling the varicose ulcer and appearing on the face, back of hands and forearms, or on the lower extremities, especially on the knees and shins. This phagedenic ulcer is characterized initially by the development of papulovesicular lesions that rupture and form painful crusted purulent ulcers. The condition probably represents an infected ulcer from some secondarily antecedent neglected lesion. Etiology is uncertain. It occurs in various desert regions of Africa, Australia and the Near East. Its relationship to tropical ulcer is not established.

Tumoral Calcinosis:

Also called exudative calcifying fasciitis and calcium gout. The disease is a condition marked by the deposition of calcium salts in nodules in various tissues of the body, especially in the subcutaneous tissues, muscles, tendons, and nerves. The lesions are characterized by a development of periarticular masses, usually present as slowly growing tumors over pressure points such as the shoulder, elbows, buttocks or hips. They may be multiple and vary from 1 to 8 cm in diameter. Involvement of underlying muscle is not uncommon. Features of tumoral calcinosis are frequently multilocular cysts of fluid containing hydroxyapatite $[3\text{Ca}_3(\text{PO}_4)_2\text{-Ca}(\text{OH})_2]$ crystal clusters with marked calcification surrounded by a fibrous capsule and giant cells (Thomson and Path, 1966; James *et al.*, 1976). McClatchie and Bremner (1969) described some of these larger calcifying foci as arising in degenerative bundles of collagen. The occurrence of benign calcified lesions in the subcutaneous tissues around the hips, buttocks and shoulder girdle was described by Inclan (1943). The disease is marked by symptoms such as sciatica due to pressure on adjacent nerves. Some cases have been diagnosed by routine radiography (Palmer, 1966). The pathogenesis of these lesions is unknown, but must be related to local factors, as there is no disturbance of calcium metabolism. It is of unknown etiology, with the onset usually in the first or second decade of life. Palmer (1966), and McClatchie and Bremner (1969) reported a number of cases from different parts of Africa. The majority of cases occurs in African people, but other ethnic groups may be affected. In the tropics it is important to differentiate this condition from calcification of a dead worm in the subcutaneous tissue. A calcified degenerative *Onchocerca* and calcification in bursae may simulate this lesion (Maathuis and Koten, 1969). A different case but with similar

manifestations has been reported in Japan (Kubo *et al.*, 1992). Ethnical factors and life style, especially food habits are important to find out the pathogenesis.

Eclampsia:

Also called toxemia of pregnancy. Toward the end of pregnancy, salt retention, edema, albuminuria, and hypertension develop in about 6% of women. This syndrome is called toxemia of pregnancy or preeclampsia. The most severe manifestation of eclampsia is accompanied by convulsions and coma, but rarely coma alone, occurring in a pregnant or puerperal woman, associated with hypertension, edema, and proteinuria. There are extensive intravascular coagulations with fibrin thrombi and focal necroses in the liver (Arias and Jimenez, 1976) and other organs, kidneys, and brain, and jaundice (Iber, 1965). Histopathological findings of the liver in eclampsia are fundamentally edematous change; sinusoidal dilatation and inflammatory exudate with Kupffer cell mobilization. Liver cell cords are atrophic and show irregular structures and pleomorphism of liver cell nuclei. Degenerative or necrotic liver parenchyma are observed in intermediate and outer zones of hepatic lobules, while centrilobular areas remain intact. Eclampsia is a condition occurring in malnourished mothers in the tropics. Not only genetic predisposition but also socioeconomic conditions are important to obtain the pathogenesis.

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REFERENCES

- 1) Andrade, C. (1952): A peculiar form of peripheral neuropathy. Familiar atypical generalized amyloidosis with special involvement of the peripheral nerves. *Brain*, 75, 408–427.
- 2) Arias, F. & Jimenez, R.M. (1976): Hepatic fibrinogen deposits in pre-eclampsia. *N. Engl. J. Med.*, 295, 578–582.
- 3) Basset, A. (1969): Tropical phagedenic ulcer. pp. 25–33. *In* Simons, R.D.G.Ph. & Marshall, J. (ed.). *Essays on Tropical Dermatology*. Vol. I. Excerpta Medica. Amsterdam.
- 4) Browne, S.G. (1961): Ainhum. A clinical and etiological study of 83 cases. *Ann. Trop. Med. Parasit.*, 55, 314–320.
- 5) Clark, M. (1948): Lymphostatic verrucosis in the Fort Hall district of Kenya. *Trans. Roy. Soc. Trop. Med. Hyg.*, 42, 287–290.
- 6) Donohugh, D.L. (1963): Tropical eosinophilia. An etiologic inquiry. *N. Engl. J. Med.*, 269, 1357–1364.
- 7) Findlay, G.H. (1951): Ainhum with special reference to involvement of fingers. *Trans. Roy. Soc. Trop. Med. Hyg.*, 44, 747–754.
- 8) Iber, F.L. (1965): Jaundice in pregnancy - a review. *Am. J. Obst. & Gynec.*, 91, 721–753.
- 9) Inclan, A. (1943): Tumoural calcinosis. *J. Am. Med. Ass.*, 121, 490–495.

- 10) James, W., Harkess, M.B., & Ch, B. (1976): Tumoral calcinosis: A report of six cases. *J. Bone Joint Surg.*, 49 (A), 721–731.
- 11) Kubo, K., Manabe, J., Matsumoto, S., Kawaguchi, T., & Kitagawa, T. (1992): Unusual huge intramuscular granuloma with calcium phosphate crystal deposition in the buttock. *Acta Pathol. Jpn.*, 42, 508–511.
- 12) Maathuis, J.B. & Koten, J.W. (1969): Kikuyu-bursa and tumoral calcinosis. *Trop. Geogr. Med.*, 21, 389–396.
- 13) McClatchie, S. & Bremner, A.D. (1969): Tumoural calcinosis - an unrecognised disease. *Brit. Med. J.*, I, 153–161.
- 14) Neva, F.A. & Ottensen, E.A. (1978): Tropical filarial eosinophilia. *N. Engl. J. Med.*, 298, 1129–1131.
- 15) O'Brien, J.P. (1972): Desert Sore. pp.610–611. *In* Hunter, G.W., III, Frye, W.W. & Swartzwelder, J.C. (ed.). *A Manual of Tropical Medicine*. W.B. Saunders Co., Philadelphia.
- 16) O'Brien, J.P. (1976): Tropical ulcer. pp.666–667. *In* G.W. Hunter, III, J.C. Swartzwelder & D.F. Clyde (ed.). *Tropical Medicine*. 5th ed. W.B. Saunders Co., Philadelphia.
- 17) Oomen, A.P. (1969a): A reconsideration of the problem of elephantiasis. *Trop. Geogr. Med.*, 21, 225–235.
- 18) Oomen, A.P. (1969b): Studies on elephantiasis of the legs in Ethiopia. *Trop. Geogr. Med.*, 21, 236–253.
- 19) Ottensen, E.A., Neva, F.A., Paranjape, R.S., Tripathy, S.P., Thiruvengadam, K.V. & Beaven, M.A. (1979): Specific allergic sensitization to filarial antigens in tropical eosinophilia syndrome. *Lancet*, I, 1158–1161.
- 20) Pacheco, G. & Danaraj, T.J. (1963): Ethanol extracts of various helminths in a complement fixation test for eosinophilic lung (tropical eosinophilia). *Am. J. Trop. Med. Hyg.* 12: 745–747.
- 21) Palmer, P.E.S. (1966): Tumoral calcinosis. *Brit. J. Radiol.*, 39, 518–525.
- 22) Price, E.W. (1972): The pathology of non-filarial elephantiasis of the lower legs. *Trans. Roy. Soc. Trop. Med. Hyg.*, 66, 150–159.
- 23) Siegal, S. (1945): Benign paroxysmal peritonitis. *Ann. Intern. Med.*, 23, 1–21.
- 24) Sohar, E., Gafni, J., Pras, M. & Heller, H. (1967): Familial Mediterranean fever: a survey of 470 cases and review of the literature. *Am. J. Med.*, 43, 227–253.
- 25) Thomson J.G. & Path, F.C. (1966): Calcifying collagenolysis (tumoural calcinosis). *Br. J. Radiol.*, 39, 526–532.
- 26) Webb, J.K.G., Job, C.K. & Gault, E.W. (1960): Tropical eosinophilia. Demonstration of microfilariae in lung, liver, and lymph nodes. *Lancet*, 1, 835–842.