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INTESTINAL LYMPHOMA: FACTORS IN PATHOGENESIS

by

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Lymphoma occurs with increased frequency in patients with cell mediated immune deficiency, regardless if acquired or congenital. Neoplasia of the upper intestinal tract, including intestinal lymphoma, follows with increasing frequency long-lasting histological sprue patterns of the bowel, also regardless of the aetiology, be it allergic or infectious. In the latter group lymphomas are the first neoplasms to appear, followed by carcinoma of the oesophagus and later of the stomach.

An increased incidence of primary intestinal lymphoma, predominantly lymphosarcoma and reticulumcellsacroma, has been found in all areas of the Middle East, where autopsies are frequently performed and surgical specimens sent for routine pathological examination. Reports of a series of such cases have been published in Iran, Iraq, Israel, Lebanon and Syria. An increased incidence has also been reported in areas outside the Eastern Mediterranean Region, as for instance in Greece and amongst the Cloreds of South Africa.

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When analysing cases of intestinal lymphoma, a clear distinction must be made between primary lymphomas developing in the gastro-intestinal tract and secondary lymphomas of the bowel, since the organs under discussion may be affected by a widespread lymphoma which originated in another location. Investigations of autopsy material in Shiraz showed that primary intestinal lymphoma is associated with severe villous atrophy of the upper small intestine in 90% of all cases.

Investigations of the bowel mucosal pattern of the population as a whole on autopsy showed the following: the atrophy starts immediately after weaning from breast milk or at the very moment the infants receive additional feeding or any other form of non-breast milk nutrition. The intestinal villous atrophy affects particularly the duodenum and jejunum and is due to infection and not to allergy. The ileal mucosa is completely normal with finger-shaped villi or leaf-shaped villi in 60% of the population, which guarantees good terminal absorption and is the reason why many people with severe upper intestinal derangement as shown on perooral biopsy have fairly good absorption patterns. Fifteen per cent of the population, however, show severe atrophy of the bowel with gyration or totally flat mucosa throughout. The changes start in early infancy and persist throughout life. The fact that the intestinal lymphoma develops mostly in the upper intestinal tract, rather than in the ileum where more lymphatic tissue is concentrated, is another piece of suggestive evidence for the relation between sprue pattern and lymphoma.

During the last ten years we studied the development of cellular and humoural immunity in marasmic infants, due either to pure malnutrition or to malnutrition secondary to intestinal infection. Intestinal atrophy in the purely malnourished group as well as xylose absorption are only moderately disturbed, while the infants with diarrhoea followed by malnutrition reveal enzyme deficiencies in the bowel as well as severe absorption difficulties.

One hundred infants of the last group were studied in an orphanage. Cell mediated immunity was determined with 2,4 dinotrochlorobenzine sensitization one to six years after they had radiologically proven thymic atrophy associated with more or less severe intestinal mucosal atrophy and diarrhoea. The

results were analysed for a relationship of cell mediated immune deficiency to birth weight, development, severity of diarrhoea in the first year of life. The results will be presented at the meeting in detail and they show that persistent absence and deficiency of cell mediated immunity is related to severe diarrhoea in the first four months of life, but not to any other factor tested for.

Primary intestinal lymphoma is a disease with clear defined clinical features consisting of loss of weight, steatorrhea, production of Heavy chain IgA in some cases, clubbing of fingers and occurrence amongst the poorer population classes of the Middle East. We believe that it occurs in a previously damaged mucosa, with severe intestinal villous atrophy and that the steatorrhea develops at the very moment the additional disturbance of the lymphomatous infiltration is added to an already damaged bowel with a very limited reserve power.

The development of intestinal lymphoma is favoured by the simultaneously existing reduction in cell mediated immunity in the population as a lymphomagenic factor. Lymphoma of the intestine occurs rarely in very primitive cultures (although this has not been definitely proven) and certainly not in highly developed nations or the wealthy classes of the Middle East. In neither of these two groups would a deficiency of cell mediated immunity pose a serious problem. Amongst the primitive cultures, infants who are not breast-fed during the first few months of life die. In the well-to-do, infants do not suffer of diarrhoea or any other debilitating infectious diseases reducing cell mediated immunity. It is in the in-between group, where infections occur and a limited number of damaged infants are saved, that the persistent deficiency of cell mediated immunity paired with persistent intestinal atrophy poses a problem.

The development of intestinal lymphoma requires probably three factors: chronic irritation of the bowel mucosa, deficiency of cell mediated immunity and an aetiological agent which is up to now unidentified. We propose that the first two factors are frequently found in the Middle East in the classes of population which suffer of intestinal lymphoma, and that their eradication will diminish the intestinal lymphoma epidemic, and that intestinal lymphoma is an excellent field for further epidemiological studies in the Region.