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Nutritional Dermatoses in Rats.

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Hitherto all scaly dermatoses produced in rats by means of diets have been broadly characterized as pellagra or pellagra-like. Failure properly and exactly to describe the scaly diseases of the rat and to differentiate one disease from another has led to confusion and controversy in the field of nutritional investigation. At least 3 scaly dermatoses can be produced in the rat and prevented or cured by nutritional means. They are due to (1) vitamin H deficiency (egg-white injury), (2) vitamin B_6 deficiency, and (3) lactoflavin deficiency.

(1) Vitamin H[1] deficiency disease is the name given to the general disorder experimentally produced in the rat by inclusion of a high proportion (15 to 40%) of egg-white in an otherwise well-balanced diet which contains all the well-known vitamins. Administration of vitamin H cures this condition. Rats kept on a diet of this kind exhibit in from 4 to 6 weeks typical symptoms of seborrheid[2] dermatitis, such as erythema, intertrigo particularly around the neck and genitalia, a brown crusting chiefly over the back that is similar to "cradle cap," and scaling that progresses from the areas of intertrigo to involve the entire surface of the body and that leads finally to a generalized exfoliative dermatitis. Generalized alopecia and exquisite pruritus are also manifest. The hind legs and the ears escape involvement. Excoriations heal slowly. Skin abscesses are rare; when present they are ecthyma-like. Mild sublingual ulcers are fairly common.

The microscopic picture reveals that in the earliest stages of the disease there is edema in the upper portion of the corium; there is also acanthosis with intercellular and intracellular edema. *Altération cavitaire* and spongiosis of the stratum spinosum precede the formation of intra-epithelial vesicles. There is a questionably increased

[1] Boas, M. A., *Biochem. J.*, 1927, **21**, 712; Parsons, H. T., *J. Biol. Chem.*, 1931, **90**, 351; György, P., *Z. f. ärztl. Fortbild.*, 1931, **28**, 377; also, *Handbuch der Kinderheilkunde* (Pfaundler and Schlossmann), Berlin, F. C. W. Vogel, 1935, **10**, 58.

[2] Moro, E., *Ekzema infantum und Dermatitis seborrhoides*, Berlin, J. Springer, 1932, p. 4.

activity of the sebaceous glands. Surprisingly little cellular infiltration accompanies the marked changes in the epidermis and the edema in the corium. The fixed connective tissue cells are increased. The connective tissue is slightly edematous and dissociated. Marked hyperkeratosis and parakeratosis are next observed, and most striking is the presence of numerous dilated and hyperemic blood vessels throughout the corium. There is no evidence of endovasculitis and no perivascular infiltration. As the skin lesions undergo involution the normal epithelium is restored with slight damage to the fibrous connective tissue but with no disturbance of the elastic fibers.

(2) Vitamin B_6[3] deficiency in rats produces the disease entity hitherto called "rat pellagra" or, better, "rat acrodynia." Rats kept on a diet devoid of the vitamin B complex and supplemented with vitamin B_1 and lactoflavin manifest in from 6 to 15 weeks symmetrical dermatitis of the peripheral parts of the body, the paws, nose, mouth and ears. There is no pruritus. Scaliness and edema are evident. Alopecia usually does not occur; at most it is slight. Abscesses form particularly around the mouth and cheeks; sublingual necrotic ulcers are not uncommon. In the advanced stages scaliness over the trunk is seen. Slight or no loss of hair accompanies the scale formation.

Microscopically hyperkeratosis is observed, but not the extreme parakeratosis of the vitamin H deficiency. The epidermis here and there displays acanthosis and spongiosis, but true intra-epithelial vesiculation is not seen. The corium differs from that seen in the disease due to vitamin H deficiency in that there is a diffuse though not marked infiltration of exudative cells. Some lymphocytes are present and an occasional leucocyte, in addition to the increased amount of connective tissue cells and the edema. A few hyperemic vessels are seen here and there but they are by no means as abundant as in the disease due to vitamin H deficiency. Secondary infection is observed, with abscesses in which there is a focal necrosis. Large numbers of polymorphonuclear leucocytes are seen in the corium as well as in the follicles.

(3) Lactoflavin[3] deficiency is produced by placing rats on an experimental diet from which only the lactoflavin component of the vitamin B_2 complex has been excluded. After 8 to 15 weeks the rats show mild but definite dandruff-like flakes or scales without or with more or less symmetrical loss of hair.

Hyperkeratosis of mild degree is observed microscopically. The

[3] György, P., *Biochem. J.*, 1935, **29**, 741.

epidermis is not particularly altered; it is perhaps slightly thickened. In the upper corium there is occasionally very slight exudation. As the disease advances, the number of follicles diminishes, and there appears to be some slight increase in the activity of the sebaceous glands.

The production by nutritional means of 3 scaly dermatoses in rats, each with a different cause, indicates that the factors of nutrition and metabolic disturbance play an important etiologic rôle in similar conditions in man.

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Relative Toxicities and Therapeutic Values of Three Chemotherapeutic Agents of the Sulphonamide Type.

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Since the original report of Domagk[1] on the protective effects of 4'-sulfonamido-phenyl azo-7-acetylamino-l-oxynaphthalene-3, 6-disulfonate of sodium (prontosil) in mice infected with *Streptococcus hemolyticus*, an extensive experimental and clinical literature[2-11] has developed on the use of this and related compounds in streptococcal and other types of infections. Nevertheless, information on the relative toxicity of these several products is either incomplete or relatively limited. Further, their therapeutic efficiencies have been only imperfectly evaluated due to lack of extensive comparative data on the therapy of bacterial infections of standard virulence.

Toxicity. The oral lethal dosages of prontosil and 4-(4'-aminobenzol-sulfonamide)-benzol-sulfonamide (Disulon) cannot be accurately established due to high tolerance and the limited gastric

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