The Use of Cortisone and ACTH in Rheumatoid Disease in Swine. (17912)

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(Introduced by K. K. Chen)

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In swine there are naturally occurring disease conditions which are somewhat similar to the so-called rheumatic or rheumatoid diseases in the human. These conditions include skin and joint manifestations as well as lesions in the heart and other visceral organs. Since these disease manifestations in swine are similar to rheumatic or rheumatoid conditions in the human, it is possible that any progress toward the understanding of the disease processes in one species may help in understanding similar processes in the other species. The clinical manifestations of rheumatoid disease in swine are quite variable. In some acute cases the body temperature may be as high as 108° F. Some of these acute cases show surprisingly few other symptoms; and they sometimes make spectacular spontaneous recoveries. Frequently there is evidence of soreness or stiffness in the legs, suggesting arthralgia or myalgia. A severe shifting lameness is sometimes seen. Affected animals may be unable or unwilling to stand or walk because of painful joints or muscles.

The skin manifestations are sometimes striking, particularly in white or light-colored animals. There may be a circumscribed erythema or the reddening may be diffuse, especially on the underside of the body. Occasionally the reddening of the skin assumes a pattern similar to the erythema annulare rheumaticum of Lehndorff-Leiner sometimes seen in the human. Subcutaneous nodules sometimes occur. In the fully developed chronic stage the joint enlargements in the legs are often conspicuous. The joint enlargement is due mainly to fibrotic periarthritis. The enlargement of the carpal joint is usually symmetrical, giving that portion of the leg a spindle-shaped appearance. The tarsal joint usually shows more enlargement medially than it does laterally. Varying degrees of ankylosis occur. The ankylosis is uusually fibrous, although bony ankylosis does occasionally occur.

The gross lesions consist mainly of increased connective tissue in and near the joint capsule, together with hypertrophy, increased vascularization and hyperemia of the synovial villi. The hypertrophic villi may largely fill the joint cavity. A membrane or pannus sometimes develops over a portion of the articular surface. Frequently there is considerable deterioration of the bone adjacent to the joint, resulting in roughening and pitting of the articular surface. Considerable deformity of the joint may occur. The gross visceral lesions are sometimes conspicuous, consisting principally of fibrinous or fibrous changes on the serous surfaces. Frequently there are extensive, firm adhesions between the visceral and parietal layers of the pericardium. Pleuritic and peritoneal adhesions sometimes occur. Vegetative formations are occasionally found on and around the auriculoventricular valves, particularly the bicuspid valve. Similar formations may occur on the semilunar valves. Microscopic examination often reveals an extensive myocarditis or pancarditis.

Since the clinical and pathological features of the disease or diseases here described in swine resemble rheumatic or rheumatoid diseases in the human, it was thought that arthritic pigs may be suitable experimental animals for determining the effects of some of the newer antirheumatic treatments. Consequently, cortisone and ACTH have been used on a few cases of naturally occurring rheumatoid type of arthritis in swine.

One pig weighing about 150 lb and showing well marked symptoms was given intra-

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muscular injections of 100 mg of cortisone daily. At the end of 4 days of treatment there was definite improvement. The treatment was continued for 3 more days making a total of 7 days. Two days after treatment was discontinued the symptoms began to return. Six days later the animal was unable to rise without assistance. After the animal had gone 31 days without treatment and had not shown any appreciable improvement, treatment with ACTH was begun. Daily intramuscular injections of 40 mg were given for 5 days without any appreciable effect.

A second hog weighing about 200 lb was given 100 mg doses of cortisone daily for 6 days. Improvement was shown on the fourth and was quite definite on the fifth day after treatment was started. There was no well marked recurrence of symptoms in this animal during a period of 30 days after treatment was discontinued.

A third shoat and a fourth one, weighing about 80 lb each were treated daily with cortisone and ACTH, respectively, in the same doses as used in the foregoing trials. On the third day of treatment both animals showed definite improvement. The one being treated with ACTH was almost free of lameness. Improvement continued in both animals during six days of treatment. Three days after treatment was discontinued both animals showed a return of symptoms. On the fifth day after treatment was stopped, the animal which had been treated with cortisone showed more marked symptoms than at any time. Treatment of this animal with cortisone was then resumed and continued for 4 days. On the third day after treatment was resumed there was definite improvement. Nine days after this treatment was discontinued, the animal was again showing marked symptoms of stiffness and lameness. The other shoat which had been treated with ACTH was showing fairly well marked lameness and stiffness 20 days after treatment was stopped.

Summary. Diseased conditions occur in swine which bear considerable resemblance to rheumatic or rheumatoid diseases in the human. Some naturally affected swine showed definite improvement following treatment with cortisone and also with ACTH. More work needs to be done before drawing conclusions as to how closely analogous are the rheumatoid conditions in swine and in the human.

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Mechanism of Increased Susceptibility to Ergot Gangrene in Thyrotoxicosis. (17913)

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Ergot gangrene in the human is still occasionally reported(1,2), but fortunately is now rare. It is usually attributable to too frequent or prolonged administration of large doses of ergot alkaloids, but occasionally follows small doses. It has often been reported in association with thyrotoxicosis(3), puerperal sepsis(4-7) and jaundice(8-11), but almost never following the use of these alka-

1. Cleveland, F. E., and King, R. L., *Bull. Mason Clinic,* 1948, v2, 19.
2. Loe, R. H., *Northwest. Med.,* 1948, v47, 190.
3. Von Storch, T. J. C., *J. Am. Med. Assn.,* 1938, v111, 293.
4. Welkoff, A. S., and Ferguson, A. D., *Am. J. Ob. and Gyn.,* 1942, v44, 331.
5. McNalley, F. P., *Am. J. Ob. and Gyn.,* 1932, v23, 367.
6. Moir, C., *Proc. Roy. Soc. Med.,* 1935, v28, 1654.
7. Olesker, N. N., *Canad. Med. Assn. J.,* 1942, v46, 168.
8. Kenney, F. R., *New Eng. J. Med.,* 1946, v235, 35.
9. Yater, W., and Cahill, J. A., *J. Am. Med. Assn.,* 1936, v106, 1625.