CHANGES IN THE RESORPTIVE POWER OF RABBIT KNEE JOINT MEMBRANES DURING THE DEVELOPMENT OF ADJUVANT-INDUCED POLYARTHRITIS

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Absorption of hippuran-I^{131} by the synovial membrane of the rabbit knee joint was studied during the development of adjuvant-induced polyarthritis. In the stage of formation of the pathological process inhibition of absorption was observed. Later during the development of the arthritic changes the resorptive power of the tissues increased. The phasic changes in resorptive power of the synovial membrane are connected with the dynamics of both local and general neuro-hormonal reactions during inflammation.

In the pathogenesis of rheumatoid arthritis – one of the most widespread forms of the collagen diseases – changes in tissue and capillary permeability play an important role [1, 2, 4, 5, 7].

Most investigators assess permeability by the resorptive power of the tissues. It is obvious that in such a case it is possible to speak only of the "resultant capillary permeability," due not only to the structure of the capillary membranes but also to the state of the microcirculation, the various pressure gradients, and so on [3].

The writer has studied the resultant permeability of the synovial membranes of joints in animals in various stages of development of adjuvant polyarthritis, a condition now regarded as the most suitable model of human rheumatoid arthritis [9-11].

EXPERIMENTAL METHOD

The resorptive power of the synovial membranes was assessed with the aid of hippuran-I^{131}, which is not metabolized by the thyroid gland and which is excreted rapidly by the kidneys [6]. Hippuran-I^{131}, in a dose of 10-12 μCi in 0.2 ml physiological saline, was injected into the left knee joint of rabbits. Absorption of the isotope was monitored by means of a scintillation counter placed above the joint. The time taken for radioactivity of the joint to fall by 50% was determined.

Adjuvant polyarthritis was produced (in conjunction with A. I. Zol'nikova) in 100 chinchilla rabbits weighing 2500-3600 g by injecting adjuvant of the Freund type into the region of the medial aspects of both knee joints subcutaneously in a dose of 0.7-0.8 ml/kg body weight. The appearance of leukocytosis in the blood, a raised ESR, an increase in the concentration of C-reactive protein and sialic acids in the blood, a positive reaction to the latex test, and so on, as well as the results of postmortem examination of the animals (undertaken by V. I. Popov) on the 7th, 30th, 50th, and 90th days after injection of the adjuvant, showed that a systemic disease characterized by multiple exudative-proliferative lesions of the joints, starting with vasculitis in the synovia and later producing destruction of the cartilage (usually after the 30th day) with the formation of a "pannus" (after the 50th day), had been produced in all the rabbits.

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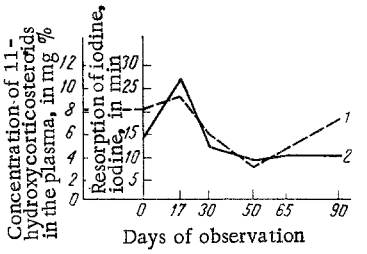

Fig. 1. Dynamics of plasma 11-hydroxycorticosteroid level and of half-elimination period of hippuran-I^{131} from the knee joint (2) in rabbits with adjuvant polyarthritis. Abscissa, days after injection of adjuvant; ordinate, on the left: concentration of 11-hydroxycorticosteroids (in mg %), on the right: resorption (in min).

EXPERIMENTAL RESULTS

From the first weeks after injection of the adjuvant into the rabbits the development of a pathological process was observed. On the 16th-17th day all the animals had a raised rectal temperature (on the average by 1°C), leukocytosis (by 44%), and increased values of the diphenylamine test (by 23%), and a raised ESR (by 67%). The knee joints were enlarged, edematous, and painful on palpation; the skin temperature above them was on the average 1.3°C higher than initially. Absorption from the knee joint cavity was delayed. The time of resorption of 50% of the radioactive isotope in 8 of the 10 animals was increased from 14 ± 0.76 min in the control to 27 ± 3.8 min.

On the 30th day after injection of the adjuvant the general and local pathological process in the rabbits was increased in severity. The animals lost weight and remained motionless. The leukocyte count in the blood was raised by 73%, the value of the diphenylamine test by 26%, and the ESR by 33%. The joints of the fore and hind limbs were painful on palpation and edematous. The skin temperature above the knee joints was raised. Unlike the previous investigation, the absorption of I^{131} from the joint was accelerated in 7 of the 10 rabbits: the half-elimination period of the isotope was 12.5 ± 0.9 min in these animals. In three rabbits the rate of absorption of I^{131} was slowed.

On the 50th day of the disease the rabbits ceased to lose weight and became more active. The rectal temperature remained elevated by 0.4°C. The blood leukocyte count was increased by 49% and the value of the diphenylamine test by 30%. The ESR was raised by 33%. Most joints (knee, hip, shoulder) remained tender on palpation and their temperature was raised. The half-elimination period of the isotope from the knee joint was considerably reduced in 7 of the 10 rabbits to 9.8 ± 0.7 min. In the animals with delayed absorption of I^{131} the clinical features of the disease were less well defined.

On the 90th day of the disease the rabbits gained a little in weight and became more active. Their rectal temperature was increased by only 0.2°C. However, the other indices reflecting the pathological process remained at their former level. Absorption of the isotope from the knee joint also remained quickened. A decrease in the half-elimination period of the isotope was observed even in the three rabbits in which it had previously been increased. This was in harmony with the increase in their leukocyte count in the peripheral blood and their raised ESR.

The phasic character of the changes in the rate of absorption of I^{131} by the connective-tissue structures of the articular membranes in polyarthritis as described above can be explained by the phasic character of the reactions developing during inflammation [8]. On the 17th day of development of adjuvant polyarthritis there is evidently a phase of increase of hydrostatic pressure and a decrease in the rate of the blood flow in the capillaries of the synovial tissue in the absence of any marked lesion in the blood vessel walls. Under those conditions delayed absorption of materials injected into the joint is easily explained. The later periods of adjuvant polyarthritis are characterized by severe lesions of the capillaries of the synovial membrane, leading to accelerated resorption of substances injected into the joint cavity.

The resorptive power of the tissues is influenced by the blood glucocorticoid level. During the development of adjuvant polyarthritis in rabbits, the author, in conjunction with A. I. Zol'nikova, observed phasic changes in the plasma 11-hydroxycorticosteroid concentration, running parallel with changes in the resorptive power of the joint tissues (Fig. 1).

The changes in resorptive power may thus be connected with the dynamics of both local and general (neuro-humoral) manifestations of inflammation.

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