largely prevents the appearance of castration cells in castrate males, when it is continued from the time of operation until the animals are killed one month later. We therefore conclude, provisionally, that the compound either directly interferes with the production of gonadotrophins by the pituitary, or else affects the presumed hypothalamic control of that function.

Atrophic changes have been detected in the testes and accessory sex organs of dogs given the compound, and in female rhesus monkeys inhibition of menstruation results from its daily administration. We have been unable to obtain any clear evidence of endocrine effects from the compound in mice, guinea pigs, rabbits or horses.

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Permeability of the Synovial Membrane to Glycoproteins

Electrophoretic investigations have indicated differences in glycoprotein pattern between serum and synovial fluid[1-3]. The most marked difference is that the relative amount of α_2-glycoproteins is considerably less in synovial fluid than in serum. It was recently demonstrated[4] that the low α_2-content of rheumatoid arthritic synovial fluid is mainly due to the low concentration of haptoglobin. The synovial fluid–serum ratio for this glycoprotein was significantly lower than for albumin or γ-globulin. The concentration of the small-molecular glycoprotein orosomucoid was, on the other hand, that expected from the total protein content, indicating a varied permeability of the blood-synovial fluid barrier to glycoproteins.

Therefore, it appeared of interest to extend the investigations to the glycoprotein permeability of the synovial membrane under normal conditions as well as in other cases with joint effusion. Since it has recently been demonstrated[5] that certain coagulation factors appear to be absent from normal bovine synovial fluid, determinations of the coagulation factors prothrombin and proconvertin, which are known to be glycoproteins, were also included in the present work.

Using previously described methods, synovial fluid-serum ratios for haptoglobin[6], orosomucoid[7], prothrombin and proconvertin[8], and certain electrophoretic protein fractions[3] were determined in cases without evidence of joint disease as well as in cases of osteoarthritis and rheumatoid arthritis. The effect of intra-articular administration of corticosteroids was also studied.

The results are summarized in Table 1. The synovial fluid–serum ratios for haptoglobin and prothrombin–proconvertin are seen to be extremely low in the cases without joint involvement (group I *a*) but increase moderately with increasing degree of synovial inflammation. Following intra-articular administration of hydrocortisone in rheumatoid arthritic cases the ratios for haptoglobin and prothrombin–proconvertin decrease markedly. The ratio for orosomucoid, on the other hand, is seen to be closely similar to that for albumin in the various groups.

The cases of group I *b* (Table 1) deserve special mention. In these cases the synovial fluid was of normal amount and appearance and there was no evidence of joint disease. However, in contrast to the cases collected in group I *a*, the patients of group I *b* presented abnormal serum protein patterns, markedly increased serum-level of haptoglobin and orosomucoid, as well as elevated erythrocyte sedimentation-rate. The changes in the synovial fluid–serum ratios for some of the glycoproteins observed in this group were of a degree found in mild synovitis and may possibly reflect a general change in connective tissue permeability to glycoproteins in infectious conditions.

The results indicate that under normal conditions the synovial membrane is very slightly permeable to certain glycoproteins. This semipermeability is obviously not related to the molecular size of the glycoprotein. Already slight synovial inflammation causes marked changes in glycoprotein permeability, which therefore should be a sensitive index of the degree of inflammation. The mechanism of the selective permeability remains unclarified.

Table 1. Synovial Fluid – Serum Ratios of Various Protein Fractions in Cases with and without Joint Disease

Group	No. of cases	Vol. of synovial fluid (ml.)*	Synovial fluid – serum ratios: Glycoproteins: Haptoglobin	Glycoproteins: Orosomucoid	Glycoproteins: Prothrombin-proconvertin	Electrophoretic fractions: Albumin	α_1	α_2	β	γ
I Cases without joint involvement										
(*a*) Without evidence of inflammatory disease	5	0·2–0·3	0·03	0·39	0·10	0·43	0·23	0·13	0·23	0·23
(*b*) With evidence of inflammatory disease (pyelonephritis)	2	0·2–0·3	0·18	0·72	0·27	0·65	0·53	0·35	0·36	0·48
II Osteoarthritis	6	0·5–10	0·24	0·64	0·18	0·46	0·45	0·21	0·32	0·33
III Rheumatoid arthritis										
Untreated	5	10–50	0·38	0·52	0·36	0·57	0·60	0·39	0·51	0·62
After hydrocortisone†	5	2–8	0·18	0·50	0·16	0·58	0·49	0·28	0·42	0·63

* As judged from the amount obtained on puncture.
† Puncture 4 days after intra-articular administration of 50 mgm. hydrocortisone acetate.

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