so as to permit one of us to give evidence at the judicial inquiry. There can be no doubt that experiments more scientifically carried out, on larger numbers of men, would give more definite results. Moreover a careful investigation of the vasomotor and other changes involved might throw light on the causes of headache. This can hardly be due to a sudden increase in the alkalinity of the tissues. For J. B. S. H. has frequently overbreathed so as to render himself so alkaline as to develop tetany and excrete a urine containing so much bicarbonate as to froth on adding acid. This has never produced a headache. On the other hand on one occasion he produced a severe acidosis with NH_4Cl. He then ate about 40 g. of $NaHCO_3$ to restore his pH to normal. This produced a severe but transitory headache, perhaps analogous to that here described.

SUMMARY

After breathing air with a partial pressure of over 6 per cent. of CO_2 for an hour or longer, five men experienced headache on breathing oxygen, and two of them vomited. The bearing of this observation on escape from submarines is discussed.

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ANTITUMORIGENIC ACTION OF PROGESTERONE

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UTERINE and extra-uterine abdominal fibromyomas produced in the guineapig by subcutaneous injection of follicular hormone develop in the non-castrated female with less constancy and in a lesser degree than in the castrated female (Lipschütz and Iglesias 1938, Lipschütz and Vargas 1939a and c). The difference in behaviour of castrated and non-castrated females is statistically significant (Lipschütz, Murillo, Vargas, and Koref 1939) and suggests that the antitumorigenic action of the ovary is due to the luteal hormone. This is corroborated by the following experiments.

Five castrated female guineapigs (225–475 g.) received subcutaneous injections of 80 μg. of œstradiol (the benzoic ester in olive oil) thrice weekly. Two of these animals were treated for 47 days and three for 90 days. All the animals revealed at autopsy uterine or extra-uterine tumours (figs. 1 and 2).

Five castrated female guineapigs (385–510 g.) were treated in the same way and with similar quantities of the benzoic ester of œstradiol. After 30 days three subcutaneous injections of 12 mg. of progesterone in olive oil were given weekly besides the 80 μg. of œstradiol. Two animals were killed after 47 days and three after 90 days. Only one animal (treated for 47 days) developed uterine tumours (fig. 3); there were no tumours, uterine or extra-uterine, in the four others. The total quantities of progesterone given were 84 mg. in 17 days and 288 mg. in 60 days; the relation between œstradiol and progesterone per injection was 1 to 150.

Most female guineapigs treated for two to three months with an ester of œstradiol show, besides uterine and extra-uterine tumours, also a remarkable development of hard fibrous tissue in the mesentery,

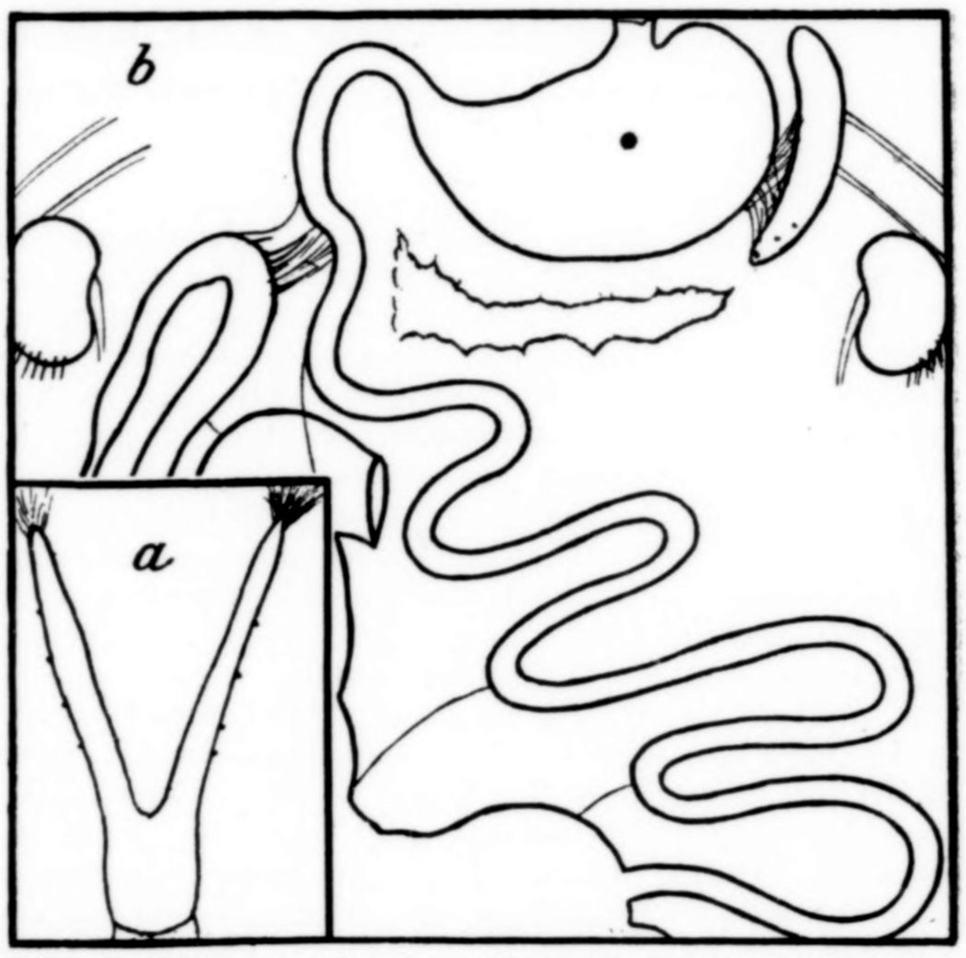

FIG. 1—Diagram showing sites of uterine and extra-uterine fibroids in a castrated female guineapig which had received œstradiol benzoate 80 μg. thrice weekly for 47 days: (*a*) small parametrial tumours, mark 0·5, and apical uterine fibrosis, mark 0·5; (*b*) fibrosis round kidneys, in mesentery, and between stomach and spleen, subserous gastric tumour, mark 1, and small tumours on surface of spleen, mark 0·5. Total mark 2·5.

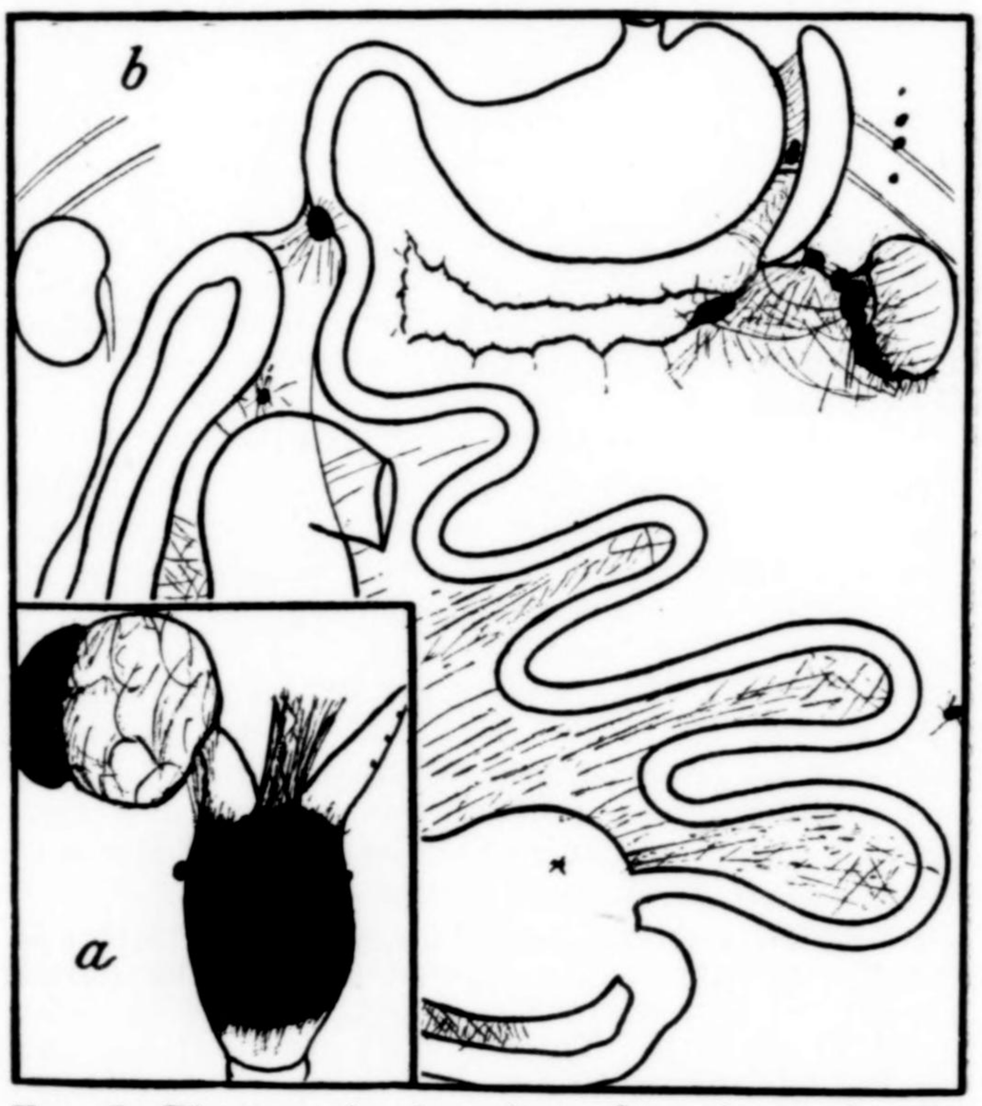

FIG. 2—Diagram showing sites of uterine and extra-uterine tumours in a castrated female guineapig which had received œstradiol benzoate 80 μg. thrice weekly for 90 days: (*a*) enormous tumour of ventral surface of uterus, mark 3, with adhesion of the epiploön, small parametrial tumours, and cystic dilatation of right tube with big tumour, mark 3; (*b*) tumours in mesentery, hilum of left kidney, and abdominal wall, mark 2, in hilum of spleen, mark 1, and fibrosis of mesentery, mark 0·5. Total mark 9·5.

round the spleen and kidneys, and elsewhere. This fibrous reaction was present also in the animals receiving œstradiol and progesterone but in a smaller degree than in those animals receiving only œstradiol.

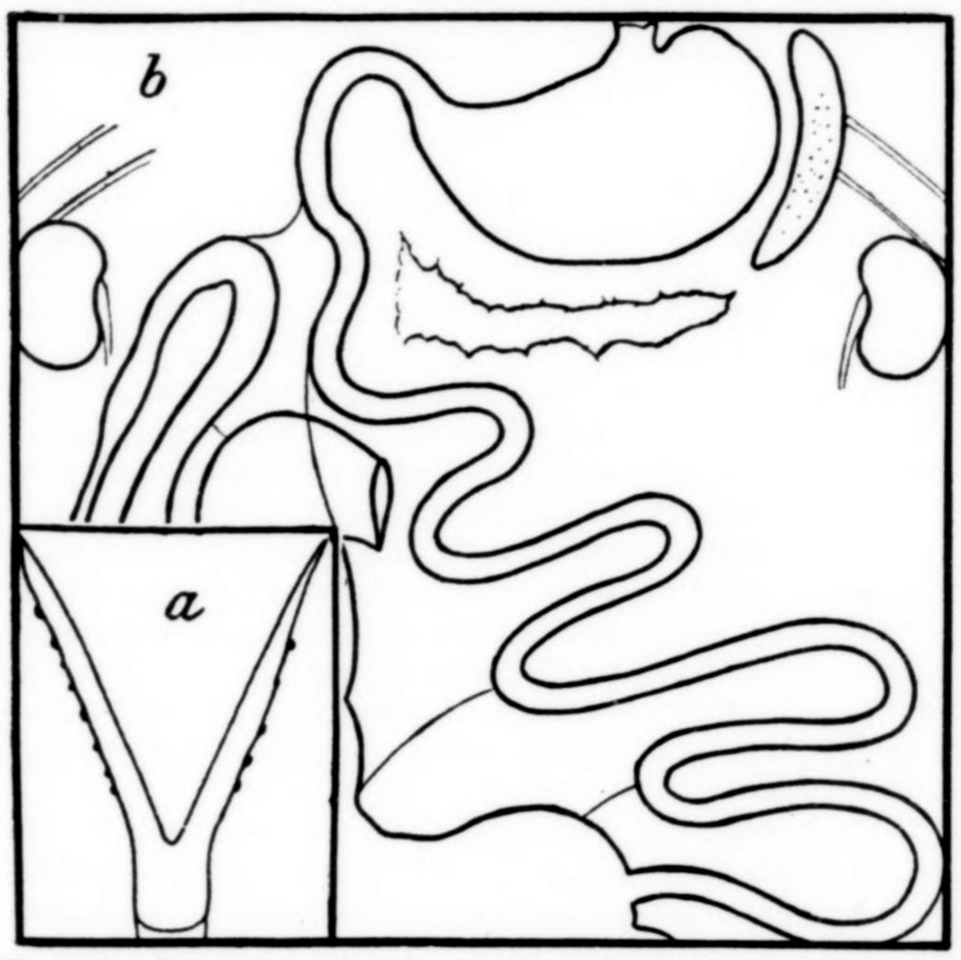

FIG. 3—Diagram showing sites of uterine and extra-uterine tumours in a castrated female guineapig which had received œstradiol benzoate 80 μg. thrice weekly for 47 days and simultaneously during the last 17 days progesterone 12 mg. thrice weekly: (*a*) small parametrial tumours, mark 1; (*b*) small tumours on spleen, mark 1. Total mark 2.

For the purpose of comparison we use a system of marks for tumours and fibrous tissue (Lipschütz and Vargas 1939b). The average mark of the group receiving only œstradiol was 4; the average mark of the group receiving œstradiol and progesterone was 1.

Our experiments with progesterone, though few, suggest strongly that this substance exerts an anti-tumorigenic action. The quantity of progesterone necessary to suppress completely the tumorigenic action of œstradiol benzoate is more than 150 times greater than that of the latter. According to Courrier and Cohen-Solal (1937) the œstrogenic action of œstradiol also is suppressed by a quantity of progesterone 200 to 400 times greater than that of the œstradiol.

Our results support the hypothesis that the development of uterine fibromyomas in women is due to a disturbance of the normal balance between follicular and luteal hormones and of their normal timing (Lipschütz 1939), and that progesterone may prove useful as a therapeutic agent against fibromyoma (*Lancet* 1939).

Our thanks are due to Messrs. Ciba, of Basle, and Laboratoires du Dr. Roussel, of Paris, for the benzoic ester of œstradiol; and to Messrs. Organon, of Oss (Holland), for the progesterone.

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AMYLOIDOSIS COMPLICATING STILL'S DISEASE

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THE following case presents unusual features in that diffuse amyloidosis developed in the course of Still's disease, there being no evidence, either during life or at autopsy, of suppuration, tuberculosis or syphilis.

CASE-RECORD

A girl aged 7 years was admitted to the Glasgow Royal Infirmary on April 21, 1932, suffering from pain and swelling of ankles and knees which had been present for six months. Her mother said that since the child had had acute rheumatism at the age of 3 years she had been subject to vague pains in the limbs.

On admission she was well-nourished but small for her age. There was some swelling of knees, ankles and tarsal joints of both feet, but no tenderness or limitation of movement. Radiography of joints showed no abnormality. Her tonsils were enlarged and the fauces were congested. The abdomen was normal and the cardiac sounds were pure. Her temperature rose to 99° F. on three occasions during her seven weeks' stay in hospital, but otherwise there was no pyrexia. The urine was normal.

In August, 1932, little change was noted on physical examination, but by November her general condition had deteriorated. Her wrists were swollen as well as her knees, ankles and tarsal joints and the tonsillar lymphatic glands had become palpable. Between November, 1932, and March, 1933, various signs appeared suggesting an "infective" source of her arthritis. For six weeks there was continuous irregular pyrexia up to 102° F. uninfluenced by sodium salicylate. On two occasions she had a fleeting erythematous rash and the spleen became palpable. She had a slight degree of anæmia (Hb. 82 per cent., red cells 4,170,000) and a polymorph leucocytosis (25,800 per c.mm., polymorphs 78 per cent.). However, by March, 1933, her general condition showed improvement. She spent the remainder of 1933 partly in hospital and partly in a children's home in the country. By the end of the year the proximal interphalangeal joints of the index and middle fingers had become affected and there was stiffness of the cervical spine. At this time her tonsils were removed.

The next three years were spent in the country. On Oct. 6, 1936, she was readmitted to the Infirmary, when it was evident that the disease had not been arrested by tonsillectomy and abundance of fresh air and sunlight. She was now 11 years old, small for her age but well-nourished in face and trunk. Her limbs had lost much muscle-substance and there was also some atrophy of the small muscles of the hands. She had a typical rheumatoid deformity of the fingers and hands. The wrists and elbows were moderately swollen and early contractures prevented full extension of these joints. There was fullness of knees and ankles with slight limitation of movement. Radiography showed osteoporosis. The lymphatic glands of neck, axillæ and groins were now palpable; the spleen had increased in size and the edge of the liver could just be felt. There was no ascites and, apart from a systolic murmur of functional type, cardiac examination was negative. Leucocytosis persisted (21,000 per c.mm. polymorphs 85 per cent.) and the anæmia had increased (Hb. 60–65 per cent., red cells 3,970,000–4,600,000). Blood-culture and Wassermann reaction were negative. The fundi were normal. In October and November she ran a