spect paid to science and scientists in the Soviet Union. Most of them were surprised by the warmth of their reception and by the fact that for the first time in the case of any visiting bourgeois group, except Ministers of State, there was a reception for the delegates of this congress within the exclusive ramparts of the Kremlin in Moscow.

WALTER DURANTY

SPECIAL ARTICLES

CRYSTALLINE PROGESTIN AND INHIBITION OF UTERINE MOTILITY IN VIVO[1]

SEVERAL years ago we[2] showed that the injection of progestin-containing extracts of the corpus luteum into post-partum rabbits caused complete suppression of the rhythmical uterine contractions usually found at that time, and also that the injection of oestrin into castrated rabbits while under the influence of corpus luteum extracts failed to induce oestrous motility. We were unable at that time to say whether the inhibitory effect of the extracts was due to the progestin or to some other hormone, since no attempt was made to study any fractions other than those known to contain progestin.

During the past year progestin has been isolated in crystalline form and its formula and structure determined.[3] Consequently, we have studied the effect of the pure hormone on uterine motility *in vivo* to determine whether or not it retains the motility-inhibiting factor which we have already shown to be present in the impure progestin-containing extracts.

The experiments were carried out in adult female rabbits whose sexual maturity was proved in most instances by the birth of one litter of young and in the remaining cases by ovulation following a single injection of pregnancy urine. Such animals were castrated and a uterine fistula prepared by transecting the vagina just below the cervix, closing the lower end and bringing the upper end through an opening in the anterior abdominal wall, where it was sutured to the edges of a small opening in the skin.[4] Several days after this operation they were given 100 rat units of Theelin, half intravenously and half intramuscularly to induce oestrous motility. Such injections have to be made because castrated animals such as these exhibit almost no spontaneous motility *per se*. The day after the Theelin was given a small rubber balloon was inserted without anesthesia into one cornu of the uterus and connected through a suitable air-water apparatus to a kymograph in such a way that the spontaneous uterine contractions could be recorded. A continuous record was then made of the oestrous type contractions for about one half hour. Progestin was next injected subcutaneously and the recording continued without interruption for 4 to 5 hours or until complete suppression of uterine motility had taken place (less than 1 hour with the larger doses).

Three different progestin preparations were used: The first was moderately pure (1 rabbit unit = 40 mgs) and the other two were crystalline, one the needle form and the other the prism form. (Progestin occurs in two polymorphous forms.) Both types of crystals gave combustion figures indicating the formula $C_{21}H_{30}O_2$, absorption spectra with a maximum at 240 mμ, and both had the same physiological potency when assayed by the Corner-Allen test for progestin.

We found that the impure extract caused complete suppression of uterine motility within 1 hour after injection when 1.2 rabbit units were given, 2 hours with 0.6 units and 4 hours with 0.3 units. Using the prisms, inhibition was obtained in 3¾ hours from 0.2 rabbit unit (0.26 mg) and in 2½ hours from 0.4 unit. Similar results were obtained when the other type (long needles) were injected.

These results indicate that there is no difference physiologically between the two forms of crystals, either form being capable of suppressing uterine motility, and further, since the pure hormone possesses the same inhibition capacity per rabbit unit as an impure extract, it is evident that both reactions, *i.e.*, inhibition of motility and progestational proliferation of the endometrium, are brought about by action of one and the same hormone.

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[1] Aided by a grant from the Therapeutic Research Committee of the American Medical Association.

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A COLLOIDAL DYE EFFECTIVE IN TREATING PERNICIOUS ANEMIA AND EVOKING RETICULOCYTOSIS IN GUINEA PIGS[1]

WE have confirmed the observation of Massa and Zolezzi[2] that the intravenous injection of repeated

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doses of the mono-azo dye, Congo Red, produces effects quite similar to those of liver extract in cases of primary anemia. Our observations were made on two cases of untreated but mild Addisonian anemia, using intravenous injections of 1.5 per cent. Congo Red 4B in 6 per cent. dextrose. One patient received 60 ccm in five days, the other 90 ccm in ten days; both had a rise in reticulocytes and a fall in serum bilirubin comparable to that produced in similar cases by intramuscular injections of liver extract. Massa and Zolezzi continued treatment until blood regeneration was complete in nine of the fourteen cases which responded to Congo Red, but we felt that liver therapy was less troublesome to administer for continuous management.

Many normal guinea pigs exhibit a slightly delayed but sharp and sustained reticulocyte shower, following injection of liver extracts known to be potent in pernicious anemia. This response seems specific for the liver fractions valuable in therapy.[3,4] Congo Red injected daily for five days into the peritoneal space of guinea pigs produced a reticulocyte shower, maximal from 5 to 7 days after beginning treatment with 30 mgm of dye per pig daily. The reticulocytosis declined gradually, reaching the control level from 10 to 14 days after the peak. At that time large doses of potent liver extract were injected, but caused no further reticulocyte response. Congo Red not only produces the same effect on normal guinea pigs as potent liver extract, but the treatment, like that with liver, renders the animals refractory to liver therapy for a considerable period of time.

These results of injecting a mono-azo dye with colloidal properties can scarcely be accounted for by the widely current theory that pernicious anemia is cured, and the reticulocyte response of guinea pigs evoked, by providing a substance needed for the maturation of red corpuscles. Massa and Zolezzi[5] suggest that the dye prevents hemolysis by blocking reticulo-endothelial cells. While the theory that pernicious anemia results from over-active blood destruction and can be corrected by blocking the reticulo-endothelial system might be satisfactory to account for the blood disturbances of Addisonian anemia, it obviously fails to account for the glossitis and spinal cord lesions which often accompany the disease and are arrested by liver therapy. Congo Red is notably effective in neutralizing toxic substances (curare, strychnine, diphtheria and tetanus toxins) and it is more probable that in pernicious anemia and in normal guinea pigs it assists in detoxification of substances, probably enterogenous in origin, which are hemolytic. These observations make imperative a further exploration of the old theory that pernicious anemia is due to excessive absorption or deficient detoxification of noxious substances derived from the gastro-intestinal tract. While it is not improbable that the effective factors in liver are utilized in the detoxification of a toxin, it seems highly unlikely that Congo Red can supply material needed for production or maturation of red cells or for maintenance of neurones and lingual papillae.

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DEUTERIUM AS AN INDICATOR IN THE STUDY OF INTERMEDIARY METABOLISM

MANY attempts have been made to label physiological substances by the introduction of easily detectable groups such as halogens and benzene nuclei. However, the physical and chemical properties of the resulting compounds differ so markedly from those of their natural analogues that they are treated differently by the organism. The interpretation of metabolic experiments involving such substances is therefore strictly limited.

We have found the hydrogen isotope deuterium to be a valuable indicator for this purpose. The fact that it occurs in the same proportion (1 atom of deuterium to 5,000 atoms of protium) in the hydrogen of ordinary water and of organic matter is in itself evidence that the living body is unable to distinguish the few organic molecules which contain deuterium from those which do not. Were the reverse the case, organic matter of biological origin would display differences in isotopic ratio.

We have prepared several physiological compounds (fatty acids and sterol derivatives) containing one or more deuterium atoms linked to carbon, as in methyl or methylene groups. Their physical properties are indistinguishable from those of their naturally occurring analogues by the methods commonly employed. As, however, the deuterium content of these substances or of their physiological derivatives can readily be determined from the properties of the water formed on combustion, their fate in the body can be followed even after considerable dilution.

In preliminary feeding experiments with different amounts of fat (linseed oil, partially hydrogenated with deuterium; the product had similar properties to olive oil) to mice, it was found that most of the fat, before being utilized, is stored in the fat depots; the fat burned in the body was not taken directly from that absorbed but from the fatty tissue.