The question still remains: what is the exact source of these auxines? Since a biochemical study of the phenomenon, which might be undertaken by means of a pure culture of uromyces, has as yet not been atempted, it is at present only possible to suggest a hypothesis: (a) that the fungus makes the auxines from which the level of the auxines in the parasitised tissues is augmented, or (b) that the diseased plant reacts by making an excess of auxines, or (c) that the parasite, by the formation of special bodies, causes the activation of the precursors of the auxines.

Comparative Antifibromatogenic Action of Progesterone and Δ^{11}-dehydroprogesterone

Among the different derivatives of progesterone with a double bond Δ^{11}-dehydroprogesterone offers a special interest. When first prepared (SHOPPEE and REICHSTEIN[1]; HEGNER and REICHSTEIN[2]; VON EUW and REICHSTEIN[3]) it was found to be progestational; but due to the small quantities of the compound then available, no exact knowledge about its progestational potency was obtained. More recently the group of WETTSTEIN (MEYSTRE *et al.*[4]) were successful in preparing the Δ^{11} compound in larger quantities; the Δ^{11} compound was shown to be 3 times as progestational as progesterone in the rabbit test. Thus the Δ^{11} compound apparently is the most active "gestagen", to use MIESCHER's[5] terminology.

Progesterone is known so far to be the most potent antifibromatogen (LIPSCHUTZ and VARGAS[6]; LIPSCHUTZ *et al.*[7]; LIPSCHUTZ[8]). However, antifibromatogenic potency is not concomitant with progestational potency; when the progestational potency of androgens is increased by substitutions at C_{17} their antifibromatogenic potency does not increase correspondingly (LIPSCHUTZ[9]; LIPSCHUTZ *et al.*[10]; LIPSCHUTZ[9]). Compounds of more or less equal progestational potency may differ very considerably as to their antifibromatogenic potency as, for instance, methyldihydrotestosterone and ethinylandrostenediol (IGLESIAS *et al.*[11]; see also MASSON and SELYE[12]). Thus it seemed of considerable interest to examine the following two questions: (1) will the Δ^{11} compound share with progesterone the faculty to prevent oestrogen-induced abdominal fibroids in the guinea-pig; and (2) will the antifibromatogenic potency of the Δ^{11} compound increase with the progestational one?

Experiments.—The results obtained with 30 castrated female guinea-pigs receiving simultaneously oestradiol and the Δ^{11} compound are summarized in the Table. The Δ^{11} compound was absorbed from subcutaneously implanted pellets, or tablets, of 15 to 22 mg each; in experiments with smaller quantities half a tablet was used, or tablets containing 40% of the specific steroid and 60% of cholesterol. Absorption from mixed pellets was calculated on the assumption of non selective absorption; absorption per day was obtained by dividing loss of weight of the dried pellet by the number of days (for the errors implied see FUENZALIDA[1]; FUENZALIDA and LIPSCHUTZ[2]). For greater details in the present experiment see the footnotes of the Table. Oestradiol was absorbed from pellets of 13 to 20 mg; absorption was of 28 to 72 µg per day.

An experiment with 32 animals receiving progesterone has been used for comparison. Absorption of oestradiol was of 26 to 66 µg per day. Two groups of older experiments with 24 animals receiving small quantities of progesterone (LIPSCHUTZ *et al.*[3]) were also added. The groups Progesterone-VI and VII are distant of no less than 10 years from one another; steroids of different chemical concerns have been used. However, results were fully coincident in these 2 groups: an antifibromatogenic effect was obtained with the small quantities of progesterone absorbed in these 2 groups. Results were not inferior to those in groups Progesterone-I, II, III, and V. The antifibromatogenic threshold quantity of progesterone was thus about 13 to 20 µg.

With 1 pellet of the pure Δ^{11} compound as in group III an absorption of about 100 µg per day was obtained, i.e. absorption rate was considerably smaller than with progesterone: 1·57 µg of Δ^{11} per mm²/day, against 4·4 µg of progesterone (the average for progesterone is 3·3; see FUENZALIDA[1]; FUENZALIDA and LIPSCHUTZ[2]). The antifibromatogenic effect was identical with that of similar quantities of progesterone. With quantities of the Δ^{11} compound somewhat above the progesterone threshold as in group V, results with the Δ^{11} compound were less secure; there was 1 animal with tumours (see coefficient Q_{2-3}). The nodules "apical" were in this animal not of the common fibroid or desmoid type of oestrogen-induced abdominal tumours but leiomyomata of the mesosalpinx; they were similar to the leiomyoma pictured in Figure 16*A* in LIPSCHUTZ[4] and included Wolffian tubules. The greater resistance of the oestrogen-induced leiomyoma against the Δ^{11} compound is of interest; so far uterine leiomyoma in women has not been made to diminish under the influence of progesterone (SEGALOFF *et al.*[5]).

With quantities beneath the progesterone threshold (group VIII) antifibromatogenic action was somewhat more pronounced with the Δ^{11} compound. However, much stress cannot be laid on this difference on account of the great variation of results in similar experiments; likewise, absorption figures are probably less exact with such small quantities than with larger quantities. Indeed, the difference between Δ^{11}-VIII and the control in IX was very considerable. But again, the tumoral effect in control groups is in general not so great as in the present case; an average of 4 to 5 is the rule.

Elsewhere we have attracted attention to the fact that even with a multiple of the threshold—about the 20-fold in our experiments with progesterone—inhibition of the

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Comparative results with the antifibromatogenic action of progesterone (32 animals) and of Δ^{11}-dehydroprogesterone (30 animals).– 24 animals with progesterone belonging to older work also have been added.

Groups	No. of animals	Steroid per day μg	Fibrous Tumoural Effect[2]	Coefficient[2] Q_{2-3}	Uterine weight gm
Progesterone[1]					
I	4	*284* (255–306)	*1·3* (1–1·5)	0	1·1 (0·5–1·5)
II	6	*144* (126–176)	*1·3* (1–1·5)	0	1·5 (1·1–2·2)
III	5	*92* (83–108)	*1·0* (1–1)	0	1·5 (1·0–2·3)
IV					
V	12	*32* (21–47)	*1·4* 0·5–1·5)	0	2·1 (0·9–2·5)
VI	5	*15* (13–19)	*1·4* (1–1·5)	0	2·5 (1·8–3·1)
VII[4]	12	*15* (13–24)	*1·5* (1·5–1·5)	0	2·9 (1·7–5·1)
VIII[4]	12	*9* (5–12)	*3·6* (1·5–8)	1·0	3·2 (1·9–5·2)
Δ^{11}-dehydroprogesterone[3]					
III	6	*102* (90–106)	*1·3* (1–1·5)	0	1·6 (0·9–2·5)
IV	4	*64* (56–70)	*1·5* (1–2)	0	2·1 (1·6–3·7)
V	8	*32* (27–37)	*1·9* (1–2)	0·25	2·2 (1·4–3·2)
VI					
VII					
VIII	12	*8* (5–12)	*2·3* (0·5–6)	0·3	2·9 (1·7–5·3)
IX	8	*0*	*6·3* (3–11)	2·1	5·1 (2·8–9·8)

[1] 1, ½, and ¼ pellet of pure progesterone in I, II, and III; 1, ½, or ¼ mixed pellet in V to VIII.

[2] A. LIPSCHUTZ and M. MAASS, Cancer Res. *4*, 18 (1944).

[3] 1 and ½ pellet of pure Δ^{11} compound in III and IV; 3 mixed pellets in V; 1 or 2 mixed pellet in VIII.

[4] These two groups belong to work formerly published (LIPSCHUTZ *et al.*, 1944) and are given for comparison. Group VI and VII are coincident as to quantities absorbed per day. It will be seen how greatly actual results coincide with those in experiments made 10 years ago. It may be seen also how satisfactorily our classification though arbitrary is working; classification of results of these older experiments has been made anew and produced the same figures as before: 1·5 instead of 1·4, and 3·6 instead of 3·4.

fibrous effect is not a complete one (see discussion in LIPSCHUTZ[1], p. 133–135). The present results give new evidence as to this (group I). Likewise, complete inhibition was not attained with the maximal quantities of the Δ^{11} compound used (group III).

The comparative action of the two gestagens on the uterus also deserves interest. Progesterone counteracts the oestrogen-induced increase of uterine weight. As the vaginal entrance becomes closed under the influence of progesterone these small uteri may become distended (IGLESIAS *et al.*[2]; see also LIPSCHUTZ[1]). All this occurred also with the Δ^{11} compound.

With reference to the uterine weight the following finding is remarkable. As seen from the table the decrease of the antifibromatogenic effect was with the threshold quantity not smaller than with the largest quantities used; on the contrary, quantities larger than the threshold quantity are necessary to counteract the abnormal increase of the uterine weight. This again applies both to progesterone and to the Δ^{11} compound.

Steroids were very generously supplied by Dr. A. WETTSTEIN, Ciba, Basel (Δ^{11}-dehydroprogesterone); by Drs. A. WHITE, Director of Research, and I. V, SOLLINS, Director, Chemical Specialities, New York, and Syntex, México (progesterone and oestradiol). Cordial thanks are due to them.

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[1] A. LIPSCHUTZ, *Steroid Hormones and Tumors* (Williams & Wilkins, Baltimore, 1950).

[2] R. IGLESIAS, A. LIPSCHUTZ, and G. NIETO, Cancer Res. *4*, 510 (1944).

Zusammenfassung

Gleich Progesteron besitzt auch das Δ^{11}-Dehydroprogesteron starke antifibromatogene Wirkung, das heisst die Fähigkeit, die Entwicklung des durch Oestradiol beim Meerschweinchen erzeugten Fibroms der Abdominalserosa zu verhindern. Die hierzu benötigten Mengen des Δ^{11}-Dehydroprogesterons betrugen, wie beim Progesteron, bloss wenige Mikrogramme pro Tag, wenn aus subkutanen Tabletten absorbiert. Die Frage, ob mit der grösseren progestativen Wirkung des Δ^{11}-Dehydroprogesterons auch eine grössere antifibromatogene Wirkung einhergeht, bleibt einstweilen offen. Auch die durch Oestradiol erzeugte abnorme Vergrösserung des Uterus wird wie mit Progesteron so auch mit Δ^{11}-Dehydroprogesteron verringert. Die Absorptionsgeschwindigkeit des Δ^{11}-Dehydroprogesterons ist um mehr als das Doppelte geringer als diejenige des Progesterons.

Die Beeinflussung der Fruktoseaufnahme des isolierten Zwerchfells durch Insulin

Aus folgenden Untersuchungen ergibt sich, dass der Umsatz von Fruktose weniger insulinabhängig ist als derjenige von Glukose:

1. Der oxydative Abbau C^{14}-markierter Fruktose durch Leberschnitte alloxandiabetischer und gesunder Ratten zeigt keinen Unterschied, während die Glukose-