THE EFFECT OF FOLLICULAR HORMONE ON NON-PATENT FALLOPIAN TUBES

BY

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In 1938 Professor Clauberg reported the results of the action of large doses of oestrin on the Fallopian tubes. His experiments were first carried out on laboratory animals. He showed that after several large doses of oestrin the Fallopian tube in an infantile animal was elongated and its lumen widened. He then applied this treatment to women whose radiographs showed a small undeveloped type of uterus and non-patent tubes. He assumed that owing to under-development the lumen of the tube might be so narrow that lipiodol failed to enter. After five injections, each of 50,000 I.B.U. of oestradiol benzoate (progynon-B oleosum forte), at five-day intervals, a second radiograph showed patency.

Clauberg's theory is that oestrin stimulation induces hyperaemia and hence increased development with expansion of the tube. He illustrated this result histologically by sections of Fallopian tubes taken from women who had undergone a course of oestrin therapy as indicated above, previous to being operated on for some gynaecological lesion. These sections showed hyperaemia and proliferation of tubal epithelium. He suggested that this treatment might be applied to improve the state of pathological tubes in cases other than those of under-development.

It was hoped that the hyperaemia induced would so soften the tubes that where fine adhesions were in existence, causing obliteration of the lumen, the further instillation of lipiodol or the insufflation of CO₂ under pressure might break them down and so effect patency.

The Present Investigation

I have carried out experiments on these lines in thirteen women, all investigations being undertaken in the out-patient department. Rubin's insufflation apparatus has been used to obtain the tracings, which are reproductions of the original ones attached to the revolving drum. With

this apparatus the insufflator is inserted into the cervix and CO₂ is turned on from a cylinder fitted to the apparatus. Taps are adjusted so that 30 c.cm. of CO₂ passes over every half-minute, and, by means of a manometer connected by a T-way fitting to both patient and cylinder, the pressure reached before patency of the tubes is attained and air is heard escaping from the ends of the tubes is shown by a kymographic tracing on a revolving drum. The waves obtained denote peristaltic contractions of the tubes.

Nine of the thirteen women had lipiodol injected into the uterus, and were found to have non-patent Fallopian tubes on x-ray examination. In none of the cases was any trace of lipiodol in the peritoneal cavity shown on the radiographic plate taken twenty-four hours after the injection. In seven of the cases the x-ray diagnosis of non-patency was confirmed by insufflation with Rubin's apparatus, but in two there was patency—in the one case at a pressure of 130 mm. Hg three months after lipiodol injection, and in the other at a pressure of 100 mm. Hg one month after lipiodol injection, showing that lipiodol *per se* has a therapeutic value. In neither of these cases were tubal contractions present, indicating rigid tubes.

Four other patients were treated who were not injected with lipiodol before starting oestrin therapy. Two had non-patent tubes at a pressure of 200 mm. Hg, and in two the tubes were patent at a pressure of 180 mm. Hg, but in none of these four cases were tubal contractions present. Each of the thirteen cases was given five injections of 50,000 I.B.U. of oestradiol benzoate (progynon-B oleosum or dimenformon) at five-day intervals, and at the end of the course—that is, in most cases one month after the last insufflation and hence at a comparable time in the menstrual cycle—the insufflation was repeated.

Results

My results are shown in Table I; the histories of two cases are reported and are illustrated with kymographic tracings before and after treatment. In every case, unless otherwise stated, examination of the husband's semen showed that this was of fertility standard; and other investigations and the past history gave no cause except non-patency of the Fallopian tubes as the possible reason of sterility on the part of the women. Except where indicated otherwise sterility was absolute.

TABLE I.—Results of Insufflation

Case	Age	Years Married	Children or Miscarriages	Birth Control	Diagram of Lipiodol in Uterus and Tubes	Insufflation before Injections	Insufflation after Injections	Kymographic Tracing	Pregnancy	Husband's Seminal Analysis
1	23	2	0	0		Non-patent 200 mm. Hg	Non-patent 200 Hg			Good
2	30	5	0	0		" 200 "	Patent 100 Hg	Good contractions	In 1 month	"
3	39	12	1 child (aged 3)	0		" 200 "	" 60 "	" "	1 month (misc.)	"
4	24	4	0	0		" 200 "	" 120 "	Poor "		"
5	30	2	0	0		³ / ₂ after radiograph patent 130 Hg. Pain left side, no contractions	" 90 "	Fair "		"
6	35	2½	0	½ yr.		Non-patent 200 Hg	" 70 "	Good "	In 6 weeks (misc.)	"
7	30	6	1 misc. 3 yrs. ago	0		¹ / ₂ after radiograph patent 100 Hg. No contractions	" 160 "	No "		"
8	26	6½	0	0		Non-patent 200 Hg	Non-patent 200 Hg			"
9	36	9	0	0		" 200 "	" 200 "			"
10	40	4	0	0		" 200 "	" 200 "			Poor
11	42	12	0	0	No radiograph taken	" 200 "	Patent 110 Hg	Good contractions		"
12	29	2	0	0		Patent 180 Hg	" 100 "	" "		"
13	30	8	0	0		" 180 "	" 80 "	Poor "		Good

Case 2.—Aged 30. Married five years; no pregnancies, no contraception. No history of pelvic disorder. 4/1/39: Radiograph following lipiodol injection showed no opaque substance in the left tube and a thread only in the right. There was none in the peritoneal cavity six hours later. 12/3/39: On insufflation tubes were non-patent at 200 mm. Hg pressure. There was midline pain, but no shoulder pain (shoulder pain is experienced when the tubes are patent and gas collects under the diaphragm, causing referred pain to one or both shoulders). 10/5/39: Following a course of five injections as indicated above, tubes were patent, giving good

* Pressure released. † Pressure reapplied.

FIG. 1.—Case 2. Kymographic tracing before injection (15/3/39).

FIG. 2.—Kymographic tracing of Case 2 after five injections of 50,000 I.B.U. of oestradiol benzoate (10/5/39).

contractions at 100 mm. Hg pressure. Bilateral shoulder pain was experienced. 10/12/39: Patient five months pregnant. Last menstrual period, June 18.

Case 6.—Aged 35. Married two and a half years. No pregnancies. Used contraceptives first six months. 21/6/39: Radiograph following lipiodol injection showed the left tube blocked at the isthmal end, the right tube dilated at the fimbrial end, and no opaque substance in the peritoneal cavity after twenty-four hours. 19/7/39: On insufflation,

tubes were non-patent at a pressure of 200 mm. Hg. Pain was experienced on the right side of the pelvis. 16/8/39: Tubes now patent and showing normal contractions at a pressure of 70 mm. Hg. Pain was experienced on the left side during the beginning of insufflation. On auscultation with a stethoscope, gas was heard apparently coming from both tubes, and she later experienced right-sided shoulder pain. 19/9/39: The patient reported she was having a heavy period, which was two weeks overdue. Menstruation had always been regular. It is possible this was an early miscarriage.

* Pressure released. † Pressure reapplied.

FIG. 3.—Case 6. Kymographic tracing before injection. Right-sided pelvic pain was felt (19/7/39).

FIG. 4.—Kymographic tracing of Case 6 after injections (16/8/39). Air was heard coming from both tubes. Right shoulder pain was felt.

Summary of Results

Thirteen cases in which the Fallopian tubes were non-patent or only slightly patent (four cases) were given a course of five oestradiol benzoate injections, each of 50,000 I.B.U. at five-day intervals. Four of the seven cases in which non-patency of the Fallopian tubes was confirmed both by radiographs and by insufflation acquired patent tubes, with good tubal contractions in three cases and poor contractions in one case. Three of these women became pregnant, two miscarrying at six weeks. (It is assumed that in these two cases an early miscarriage took place, as the missed period occurred some time after cessation of the endocrine injections, and in neither case

had menstruation ever previously been more than a day or two overdue. One of the women who miscarried had continued syringing, as she had been wearing a Hodge pessary for some time.)

Of the two cases in which the tubes were shown to be non-patent on insufflation only, patency and good contractions resulted in one case.

Of the four cases in which the tubes were patent only at high pressure and showed no tubal contractions, three subsequently became patent at a lower pressure and showed tubal contractions, but these were good in one instance only.

In two of the cases in which patency resulted and good tubal contractions were obtained examination of the husbands' semen showed a poor spermatozoa count, the semen being below the standard required for successful impregnation.

It will be noted by studying Table I that the cases most likely to respond to treatment were those in which the tubal obstruction was at the fimbriated end.

Treatment of Sterility

I should like to take this opportunity of reporting the results of sixty-five further cases of lipiodol injection in conjunction with endocrine therapy in the treatment of sterility. In an earlier article (White, 1939) I quoted the results obtained in sixty-two cases. A very legitimate criticism of that investigation was the small number of cases concerned. Table II shows the results of the two groups treated by similar methods, and it will be seen how nearly the figures correspond.

TABLE II.—Results of Lipiodol Injection and Endocrine Therapy in Treatment of Cases of Sterility: Comparison of Two Series of Cases

	August, 1937, to June, 1938	June, 1938, to June, 1939
Number of cases	62	65
Husband's seminal analysis—		
Azoospermia	13%	8%
Oligospermia	8%	20.5%
Consented to examination ..	63%	75%
Non-patent Fallopian tubes ..	17.7%	20.0%
Pregnant following lipiodol injection Of the whole series	35.5%	26%
Of the possible cases	47.8%	47.2%
Average age of patients	30 years	30.8 years
Average duration of sterility ..	5.7 „	5.7 „
Miscarriages	32%	17.6%

I am much indebted to Miss Dearnley, in whose out-patient department these investigations were carried out.

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LATERAL ABERRANT THYROIDS

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Although cases of aberrant thyroids in the neck have been reported from other countries a perusal of the literature has failed to reveal a case from India. It is certain that this condition must have been seen there by others, but owing to the lack of facilities for histological examination it has escaped notice. Only in exceptional cases can a correct pre-operative diagnosis be made: this can only be done by the pathologist. Clinically this complaint is mistaken for tuberculous glands or even for lympho-sarcoma, and therefore many such cases remain undiagnosed. It is useful to have the condition in mind when examining a patient with a lump in the neck, because these lumps sometimes become malignant, as in the case here recorded—a fact which naturally alters the prognosis.

A short description of the embryology of the thyroid gland will help in the anatomical conception of these aberrant thyroids in the neck.

Embryology of the Thyroid Gland

This is a disputed matter. The older embryologists (His and others) thought that the major portion of the thyroid gland, including the isthmus, was derived from a median outgrowth of the epithelium from the floor of the pharynx and that this occasionally persisted as thyroglossal duct. The lateral lobes of the thyroid were supposed to be derived from the lateral out-pocketing of the pharynx (third and fourth branchial clefts), which normally fused with the median anlage. This view was simple enough to explain the presence of aberrant glands

Diagram of the branchial clefts. I, II, III, IV—Lateral clefts. Th.d.—Thyroglossal duct. u.b.—Ultimobranchial body; posterior continuation of pharynx. (After Kaufmann.)

as being due to a failure of the lateral portion to fuse with the median. Since the time of His we have come to know that the third and fourth branchial pouches form parathyroid glands, which differ structurally from thyroid gland, and therefore it was subsequently held that the thyroid gland developed only from the median anlage. Later investigation revealed a developmental relation between the fifth pouch and the thyroid gland. This fifth pouch was called the ultimobranchial body, and Kingsbury has proved that this body is mainly formed by continued growth activity of the posterior portion of the pharyngeal