the two groups of cases: the initial hold-up of the meal by pyloric spasm, the later rush through the imperfectly distended duodenal cap, the vigorous hyperperistalsis and rapid emptying of the stomach. Careful investigation of the history will often show that the earliest abdominal symptoms were suggestive of appendicular or colon pain, and that the pseudo-ulcer symptoms have supervened later.

3. *Appendix complicating Ulcer.*—Surgeons are well aware of the harmful effects of a chronic appendix on the clinical course of ulcer cases, and the benefit to the ulcer from the removal of the diseased appendix. A practical point arises in this connexion—namely, that an opaque meal should always include the radiological examination of the appendix, even though an ulcer has already been revealed.

4. *Colon Type.*—Some cases of spasm of the colon owe their origin to a diseased appendix. Their diagnosis is by no means easy, as it is well known that in many instances spastic colitis and caecal discomfort are to be found in those who have already submitted to appendectomy without relief. Nevertheless their recognition is of importance, for if the appendix is gravely at fault there is little chance of a cure until it is removed, and indeed treatment of the colon by lavage may entail a risk of setting up an acute appendicitis. The diagnosis may be approached on these lines: first, by tracing in the clinical history, especially of the early stages, any possible illness which in retrospect might correspond to an attack of appendicitis; secondly, by comparing the frequency or severity of the local pain in the right iliac fossa with the more general discomfort of intestinal indigestion and colitis; and, thirdly, by radiological examination. Finally, it may be borne in mind that in this type of case the appendix shares in the disorder of the colon, and the patient is to some extent predisposed towards acute appendicitis: the supervention of this does not therefore necessarily signify that the correct diagnosis has been missed.

Radiological Examination

In doubtful cases examination by means of an opaque meal may provide valuable confirmatory evidence. The points suggesting disease of the appendix are as follows: (i) tenderness of any part of the appendix under screen control; (ii) shifting of the tender point with artificial displacement of the caecum; (iii) fixation and rigidity; (iv) acute kinking; (v) the presence of concretions; (vi) variations in calibre; (vii) crenation of the mucosa and filling defects; (viii) imperfect filling or delayed emptying; (ix) complete absence of filling, especially after preliminary purgation. This last sign is not to be taken as of significance unless it is accompanied by one or more of the other signs enumerated.

Diagnosis and Results

The diagnosis of each type of disorder due to an abnormal appendix has already been discussed. A positive diagnosis may be claimed to be correct where operation reveals a diseased appendix or leads to a prompt cessation of symptoms. It is not, however, to be expected that operation in a quiet interval will always show macroscopic evidence of disease in the appendix, nor that where spasm and colitis have been present for a long time operation will necessarily cause an immediate freedom from all symptoms. Trying to estimate results from personal experience as fairly as possible, I think that a positive diagnosis of an abnormal appendix reached on the lines indicated is very seldom wrong. The results obtained by operation lead to this conclusion, which is confirmed by the fact

that of four patients who refused operation three have since suffered from acute attacks necessitating surgery. On the other hand it cannot be said that, even with the greatest care, a negative diagnosis is equally reliable, and I am aware of cases which I have passed as normal developing an acute attack within the next few months. Such errors are probably unavoidable if cases are seen only during quiescent intervals.

In children the diagnosis of a "medical appendix" is comparatively easy, and, where correctly made, operation is uniformly and completely successful in leading to a cessation of all symptoms. In them nothing could be more satisfactory. In adults the cases simulating ulcer are very successful, although they may need treatment for the duodenal irritation for some weeks after appendectomy. In the colon group many do obtain relief at once by operation, but in others in which symptoms of colitis and intestinal indigestion have been present for a long time operation will not do more than leave the way free for appropriate medical treatment to be instituted.

I express my thanks to Sir L. Barrington-Ward and my colleagues Mr. F. W. M. Pratt and Dr. H. Courtney Gage for their kind interest in the preparation of this address.

TREATMENT OF GONORRHOEA BY ULERON

A REVIEW OF 120 MALE CASES

BY

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The references in the Continental and world medical literature to the use of uleron in the treatment of gonorrhoea are numerically so formidable that an adequate review of the findings recorded is almost impossible to give. The preparation, which has the structural formula

and is described chemically as 4-(4'-amino-benzol-sulphonamide)-benzol-sulphon-dimethylamide, is a colourless substance, soluble with difficulty in water, and is put up in 0.5 gramme tablets.

First reported upon by Grütz (1937), who used it and allied preparations in a group of thirty-six patients, it was later the subject of investigation by Felke (1937), Fischer (1937), and many others. During 1938 approximately 160 articles appeared describing the results of using the preparation in gonorrhoea, most of them by Continental authorities. I will choose only five of these articles, which seem to give a general picture of what our Continental colleagues have achieved.

Mergelsberg (1938a), using a maximum of three "Stosses"—that is, short courses of treatment—separated by suitable pauses, and not exceeding a total of 12 grammes per three days, found that old gonorrhoea responded best and that results were quite good in complications. His figures are of interest: sixty-nine cases of old gonorrhoea which had preliminary irrigations gave a 77 per cent. cure. W. and K. Gennerich (1938), using similar dosage and a preliminary two to three weeks' irrigation with $\frac{1}{2}$ to 1 per cent. albargin, treated sixty-four cases (fifty-eight of them male), all of whom finally passed tests of cure: fifty-six of these responded to 1, six to 2, and two to 3 "Stosses." Fuhs and Volavsek (1938a), using a seven-day "Stoss," which the makers of the drug consider

inadvisable as leading to the possibility of toxic effects, obtained 90 per cent. cure in 133 men and 97.3 per cent. in thirty-six women. In later publications Mergelsberg (1938b) obtained improvement (on his original figures) to 87.5 per cent. cure in a group of patients irrigated with $\frac{1}{4}$ to $\frac{1}{2}$ per cent. protargol solution four times daily whenever the first "Stoss" had failed, while Fuhs and Volavsek (1938b), still using the seven-day "Stoss," record their cures as 90 per cent. in 299 men and 94 per cent. in eighty women, his total experience of the drug amounting to 486 cases.

British literature on uleron is relatively scanty. O'Hanlon (1938) recommended its use in cases not cured by sulphanilamide. Walsh (1938) in a preliminary article described its effects, on the whole favourable, in forty-three male cases of gonorrhoea. Cokkinis and McElligott (1938) quote their experiences in 150 cases and note that the product has no immediate toxic effects. They regard its ultimate curative value, however, as inferior to that of sulphanilamide. Hanschell (1938b) refers to 200 cases treated with uleron, and believes it to be more effective and safer for male gonorrhoea than sulphanilamide (ninety-nine cases). L. W. Harrison (1938) deals with its mode of application; Cokkinis (1938) describes its successful employment in non-gonococcal urinary infections. Nicol (1938) and Prebble (1938) also mention its use.

A number of articles on the use of sulphanilamide and M & B 693 have also appeared. Short of giving a complete list of these it will suffice to mention the publications of Cokkinis and McElligott (1938), who review 633 cases treated with sulphanilamide; McGregor-Robertson (1938), who analyses 100 cases similarly treated; and Bowie (1938), who reports on M & B 693. As regards the comparative value of the three drugs—sulphanilamide, M & B 693, and uleron—there seems to be a preference in this country for the first two of these, and emphasis has been laid on the fact that toxic polyneuritis may result from uleron. My own experience with uleron in over 200 cases has not included any instances of this complication, and I cannot help feeling that the incidence of polyneuritis must fall to a very low level if the recommended dosage (such as I have used) is employed.

Clinical Material and Mode of Treatment

For the purpose of the investigation a total of over 200 cases of gonorrhoea (all males) was originally put on uleron, but for this report only 120 are included. The cases omitted were those rendered statistically valueless by reason of faulty attendance. Of the 120, 100 were acute recently infected cases and twenty were infected for a longer period before beginning uleron treatment. All of the cases were found to have gonococci in direct urethral smears on the first attendance at the clinic and on the day immediately preceding uleron treatment. Daily irrigations (posterior from the outset when possible) with 1 in 10,000 potassium permanganate solution were given in all cases. The use of the urethral syringe was not advised, as I believe this instrument to be dangerous unless employed by an experienced medical man or under medical supervision.

The uleron was administered in short three-day courses separated by varying short intervals (usually nine days). Patients were given the following printed instructions as to dosage:

1st Day.—Two tablets three times after food.
2nd and 3rd Days.—Two tablets four times a day after food.

A full glass of water to be taken with each two tablets, and no eggs or salts (Glauber or Epsom) to be taken during the three days.

Thus twenty-two tablets (11 grammes) were given during each course.

On the days immediately preceding and following all uleron courses the clinical picture, a direct urethral smear (if obtainable), and a two-glass urine test were always recorded. No patient was dismissed as "cured" until he had passed the routine tests of cure (T.O.C.). The routine T.O.C. at this centre consists in all instances of three prostatic smears (the patient not having urinated for three hours and the glans penis having been well cleaned with surgical spirit), the passing of a metal sound into the bladder, urethoscopic examination, and a provocative gonococcal vaccine injection. A complement-fixation test for gonorrhoea is not done in all cases. The T.O.C. extends over a period of at least six weeks. A particularly long observation interval between "apparent cure" and T.O.C. was allowed for in this series.

Detailed Analysis of 100 Cases of Early Infection

All these cases were clinically and pathologically acute gonococcal urethritis on first attendance at the clinic. Seven had complications at the outset of treatment, which included peri-urethral abscess (one), epididymitis (two), copaiba rash (one), toxic conjunctivitis (one), retention of urine (one), and cystitis (one). Later, but before the first uleron course, a further twelve developed complications, as follows: epididymitis (five), peri-urethral abscess (two), cystitis (two), prostatitis with rheumatism (one), slight rheumatism (one), and arthritis of knees and ankles (one).

The average duration of urethral discharge before beginning uleron treatment was 17.9 days. The average interval between the first and second uleron courses was 9.2 days, and that between the second and third courses

TABLE I.—*Clinical Picture of 100 Cases on Completion of Uleron Treatment*

	Clinical Picture immediately following Course(s)			Clinical Picture after Period of Observation			Notes
	No Sign of Infection	Less Discharge	No Change	Relapse	Apparent Cure	Apparent Failure	
28 cases receiving one course only	18	9	1	1	26	1	The "relapse" case relapsed several weeks later and uleron was not repeated. The "apparent failure" defaulted
42 cases receiving two courses only	31	9	2	4	35	3	The four "relapses" and three "apparent failures" were not treated further with uleron
30 cases receiving three courses only	15	2	13	4	13	13	
Total of 100 cases receiving one, two, or three uleron courses	64	20	16	9	74	17	

10.8 days. Twenty-eight cases received only one uleron course, forty-two received two courses, and thirty received three courses. Table I gives the clinical picture of the 100 cases on completion of uleron treatment, and Tables II, III, and IV the clinical or pathological picture immediately following one, two, or three uleron courses.

Limitation of space unfortunately makes it impossible to give details of the protocols of each case (as has been done with the series of twenty chronic cases, which see). I have, however, a limited number of photographic copies of the details of the protocols of each acute case and will be pleased to supply one to any medical man who wishes it.

Table I shows in a graphic manner the effect of uleron in cases grouped according to whether they received one, two, or three courses of the drug. In contrast with this, Table II gives, so to speak, a cross-section of the results of treatment taken immediately after the first course of uleron and therefore including the total material of 100 cases. This point is mentioned here in order that no confusion should arise from the observation that in Table I sixty-four cases are seen to have had no sign of infection "immediately following the course(s)," while only forty-eight of 100 are shown in Table II to have had no sign of infection.

TABLE II.—*Clinical and Pathological Picture of 100 Cases immediately following One Uleron Course (including those who later received Further Uleron Treatment)*

	No Sign of Infection	Less Discharge		No Change
		G.C. —	G.C. +	
100 cases	48	24	14	14

It was not considered necessary to give further treatment to twenty-seven of the above cases after observing them for a few days. Another case defaulted while still infected, and is recorded (see Table I) as an "apparent failure."

Seventy-two patients received a second uleron course. This number comprises sixteen who relapsed after disappearance of discharge on the first course, three who relapsed after showing "less discharge," fourteen who remained free of discharge but whom it was thought advisable to treat further, twenty-six who showed "less discharge" but did not relapse, and thirteen who failed to respond to the first course.

TABLE III.—*Clinical and Pathological Picture of Seventy-two Cases immediately following Two Uleron Courses*

	No Sign of Infection	Less Discharge		No Change
		G.C. —	G.C. +	
72 cases	40	12	6	14

It was not considered necessary to give further treatment to thirty-eight (although four of these subsequently relapsed). Three were recorded as "apparent failures" to uleron after two courses.

Thirty received a third uleron course. This number comprises six who relapsed after disappearance of discharge following two courses, three who remained free from discharge but whom it was thought advisable to treat further, ten who showed less discharge after two courses, and eleven who failed to respond to two courses. That only eleven of the fourteen cases showing no improvement in the previous table were given a third course seems to require explanation. The three cases not treated further are accounted for as follows: (1) Case 68 failed completely to respond and was given other treatment; (2) Case 95 was given other treatment; (3) Case 100 developed urticaria after the second course, and further use of the drug was thought inadvisable.

TABLE IV.—*Clinical and Pathological Picture of Thirty Cases immediately following Three Uleron Courses*

	No Sign of Infection	Less Discharge		No Change
		G.C. —	G.C. +	
30 cases	15	2	0	13

The interpretation of the figures given above will be found under "Discussion and Conclusions."

Control Cases.—For the purpose of comparison 100 consecutive cured acute cases were taken from a previous year. All had received daily irrigations and had eventually completed the routine T.O.C. The average duration of discharge was fifteen weeks. Complications (mild and severe) occurred in 24 per cent. of these cases.

Detailed Analysis of Twenty Cases of Late Infection

Table V, which gives the protocols of each case, shows the type of case concerned and the results obtained. Fourteen patients had gonococcal complications before uleron treatment. All had a definite urethral discharge containing gonococci which had persisted despite irrigations for periods varying from six to eighty-eight weeks. The duration of discharge (in weeks), from the first day on which it was observed by the patient himself to the day on which the uleron was begun, is recorded in the table. As the series is not large, brief individual case records are given below.

Case B1 developed an acute unilateral epididymitis thirty-six weeks after attending the clinic. An acute urethral discharge had persisted. Uleron proved successful, the discharge clearing up in eight days. A second uleron course was given as a "follow-up." An eleven-weeks observation period was allowed before starting "tests of cure." All the T.O.C. were eventually passed successfully.

Case B2 was a severe prostatitis discharging freely. The first uleron course was given at the fifty-second week; the urethritis subsided and the prostate returned to normal. Two courses were given.

Case B3 had a persistent gonococcal urethritis due to severely infected urethral follicles. Two uleron courses produced an "apparent cure" in eleven days. A prostatitis existed at an earlier date in this case.

Case B4, with a Tyson's gland infection and a persistently discharging peri-urethral abscess, cleared up temporarily after two uleron courses, but relapsed and did not respond to two further courses. This was a definite uleron failure.

Case B5, complicated by a double epididymitis, began uleron treatment in the twenty-second week. An improvement, both in the complication and in the urethritis, was registered after the first uleron course and an "apparent cure" after the second course. The case relapsed after a provocative gonococcal vaccine injection at the beginning of the T.O.C. The value of a large provocative vaccine injection is revealed here. This case is recorded as a uleron failure.

Case B6, also with a double epididymitis, began uleron in the twelfth week of urethritis. After the first course the discharge was less and only a few gonococci were then found in the direct urethral smear. The second course was begun after an eight-day rest and no discharge resulted; a test showed clear urine (apparent cure). The case was proclaimed "cured" after a further fourteen-weeks observation period and T.O.C.

Case B7 was very similar to B6 except that the condition was better after the first course.

Case B8 developed an arthritis of the shoulder and of one finger. Uleron treatment was begun in the twelfth week. Two courses were given, an "apparent cure" being achieved after the first.

Cases B9, B10, and B11, all with no gonococcal complication, responded permanently to the first uleron course. Two

TABLE V.—Twenty Cases of Gonococcal Urethritis in the Male Subject treated at a Late Stage with Uleron. All these Cases were on Daily Irrigations of 1 in 10,000 Potassium Permanganate from the First Attendance at the Clinic

Patient's serial number Duration (in days) of urethral discharge before attending clinic Clinical picture (including complications) on first attending clinic Gonococcal complications after first attendance but before 1st uleron course	B1 14 G.I. Rt. epid. 36 wks. later	B2 2 G.I. Prosta- titis	B3 3 G.I. Infected follicles and prosta- titis	B4 14 G.I. Tyson's abscess and peri- urethral abscess	B5 4 G.I. Rt. epid. and lt. epid.	B6 4 G.I. Lt. and rt. epid.	B7 14 G.I. Lt. epid.	B8 7 G.I. Arthritis shoulder and one finger	B9 2 G.I. —	B10 2 G.I. —	B11 7 G.I. —	B12 7 G.I. General- ized ur- thrallgia & (knee) arthritis	B13 7 G.I. Peri- urethral abscess	B14 6 G.I. —	B15 3 G.I. Prosta- titis	B16 4 G.I. —	B17 3 G.I. Toxic con- junctivitis; arthritis; prostatitis	B18 14 G.I. —	B19 7 G.I. Prosta- titis and epid. (1 side)	B20 7 G.I. Epid. (both sides)
Duration of discharge (in weeks) before 1st uleron course	88	52	32	22	22	12	14	12	14	16	14	14	19	15	11	9	10	10	6	7
Clinical picture immediately before 1st uleron course	D++	D+	D++	D±	D++	D+	D+	D±	D++	D++	D+	D+	D±	D+	D±	D±	D+	D+	D+	D±
Urin 1 and 2 before 1st uleron course	Sps, H Cl D+	Sps, Ts Cl D-	Sps, Ts Cl D±	G.C., Sps Cl D±	Sps, H Cl D±	Sps, Ts Cl D±	Sps, H Cl D-	Sps, Ts Cl D-	Sps, H Cl D-	Sps, H Cl D-	Sps, Ts Cl D-	Sps, Ts Cl D+	Sps, Ts Cl D-	Sps, Ts Cl D±	Oc, Sps Cl H	F, Ts, H Cl D-	Sps, Ts Cl D±	Sps, Ts Cl D±	Sps, Ts Cl D±	Sps, Ts Cl D±
Clinical picture immediately after 1st uleron course	Sps, H Cl D+	Sps, Ts Cl D-	Sps, Ts Cl D±	Oc, Sps Cl D±	Sps, H Cl D±	Sps, Ts Cl D±	Sps, H Cl D-	Sps, Ts Cl D-	Sps, H Cl D-	Sps, H Cl D-	Sps, Ts Cl D-	Sps, Ts Cl D+	Oc, Sps Cl D-	Sps, Ts Cl D±	Oc, Sps Cl H	F, Ts, H Cl D-	Sps, Ts Cl D±	Sps, Ts Cl D±	Sps, Ts Cl D±	Sps, Ts Cl D±
Urin 1 and 2 after 1st uleron course	Sps, H Cl D+	Sps, Ts Cl D-	Sps, Ts Cl D±	Oc, Sps Cl D±	Sps, H Cl D±	Sps, Ts Cl D±	Sps, H Cl D-	Sps, Ts Cl D-	Sps, H Cl D-	Sps, H Cl D-	Sps, Ts Cl D-	Sps, Ts Cl D+	Oc, Sps Cl D-	Sps, Ts Cl D±	Oc, Sps Cl H	F, Ts, H Cl D-	Sps, Ts Cl D±	Sps, Ts Cl D±	Sps, Ts Cl D±	Sps, Ts Cl D±
Direct urethral smear (if obtainable) on day following cessation of 1st uleron course	Sps, H Cl D+	Sps, Ts Cl D-	Sps, Ts Cl D±	Oc, Sps Cl D±	Sps, H Cl D±	Sps, Ts Cl D±	Sps, H Cl D-	Sps, Ts Cl D-	Sps, H Cl D-	Sps, H Cl D-	Sps, Ts Cl D-	Sps, Ts Cl D+	Oc, Sps Cl D-	Sps, Ts Cl D±	Oc, Sps Cl H	F, Ts, H Cl D-	Sps, Ts Cl D±	Sps, Ts Cl D±	Sps, Ts Cl D±	Sps, Ts Cl D±
Gonococcal or uleron complications following 1st uleron course. Any other notes	Dis- charge cleared																			
Interval (in days) between 1st and 2nd courses	5	5	5	5	8	8	11	8	11	—	7	7	16	8	15	13	14	7	7	12
Clinical picture immediately before 2nd uleron course	D-	D-	D-	D-	D±	D±	D±	D-	D±	D-	D-	D+	D±	D±	D±	D+	D±	D±	D±	D±
Urin 1 and 2 before 2nd uleron course	F, Sps Cl D-	Oc, Sps Cl D-	Cl Cl D-	Oc, Sps Cl D-	Oc, Sps Cl D-	Sps, Ts Cl D-	Oc, Sps Cl D-	Cl Cl D-	Oc, Sps Cl D-	Cl Cl D-	Cl Cl D-	Sps, Ts Cl D+	F, Sps Cl D-	Oc, Sps Cl D-	Cl Cl D-	F, Sps Cl D-	Sps, Ts Cl D±	Sps, Ts Cl D±	Sps, Ts Cl D±	Sps, Ts Cl D±
Clinical picture immediately after 2nd uleron course	F, Ts Cl Nil	Oc, Sps Cl Nil	Cl Cl Nil	F, Ts Cl Nil	Cl Cl Nil	Cl Cl Nil	Cl Cl Nil	Cl Cl Nil	Cl Cl Nil	Cl Cl Nil	Cl Cl Nil	Sps, Ts Cl D+	F, Sps Cl D-	Oc, Sps Cl D-	Cl Cl Nil	Oc, Sps Cl D-	Sps, Ts Cl D±	Sps, Ts Cl D±	Sps, Ts Cl D±	Sps, Ts Cl D±
Urin 1 and 2 after 2nd uleron course	F, Ts Cl Nil	Oc, Sps Cl Nil	Cl Cl Nil	F, Ts Cl Nil	Cl Cl Nil	Cl Cl Nil	Cl Cl Nil	Cl Cl Nil	Cl Cl Nil	Cl Cl Nil	Cl Cl Nil	Sps, Ts Cl D+	F, Sps Cl D-	Oc, Sps Cl D-	Cl Cl Nil	Oc, Sps Cl D-	Sps, Ts Cl D±	Sps, Ts Cl D±	Sps, Ts Cl D±	Sps, Ts Cl D±
Direct urethral smear (if obtainable) on day following cessation of 2nd uleron course	F, Ts Cl Nil	Oc, Sps Cl Nil	Cl Cl Nil	F, Ts Cl Nil	Cl Cl Nil	Cl Cl Nil	Cl Cl Nil	Cl Cl Nil	Cl Cl Nil	Cl Cl Nil	Cl Cl Nil	Sps, Ts Cl D+	F, Sps Cl D-	Oc, Sps Cl D-	Cl Cl Nil	Oc, Sps Cl D-	Sps, Ts Cl D±	Sps, Ts Cl D±	Sps, Ts Cl D±	Sps, Ts Cl D±
Gonococcal or uleron complications following 2nd uleron course: Any other notes				Repeated at- tacks of slight discharge. Seen again								Knee (arthritis still severe)				Dis- charge ceased				
Interval (in days) between 2nd and 3rd courses				90								9								
Clinical picture immediately before 3rd uleron course				D-								D+								
Urin 1 and 2 before 3rd uleron course				F, Ts Cl D±								Sps, Ts Cl D±								
Clinical picture immediately after 3rd uleron course				F, Ts, Sps Cl Cl								Sps, Ts Cl D±								
Urin 1 and 2 after 3rd uleron course				F, Ts, Sps Cl Cl								Sps, Ts Cl D±								
Direct urethral smear (if obtainable) on day following cessation of 3rd uleron course				PCs+ G.C.+ Os-								PCs+ G.C.+ Os-								
Gonococcal or uleron complications following 3rd uleron course. Any other notes				A 4th uleron course given								No re- sponse to uleron								
Time in weeks from onset of discharge to beginning of "Tests of cure" (T.O.C.)	100	60	40	Still on treat- ment	30 (Re- lapsed)	24	22	20	18	15	17	Still on treat- ment	25	22	20	16	15 (on tests)	16	17	8
Time in weeks from onset of discharge to dismissal as "cured"	108	68	48			31	30	28	26	22	22		35	18	Default	20			22	
Any special notes				Uleron failure	Uleron failure							Uleron failure								Uleron failure

G.I. = acute gonorrhoea. D++ = urethral discharge profuse. D+ = urethral discharge moderate. D± = urethral discharge slight. D- = urethral discharge nil. Ts = urine threads. Sps = urine specks. Cl = urine clear. H = urine hazy. Oc = occasional (for example, G.C. = gonococci. Os = organisms (not G.C.). ++ = very many. + = many. ± = few. - = none.

courses were given to B9 and B11 and one only to B10. Case B9 developed a slight discharge between the first and second courses.

Case B12 was a uleron failure, the drug having practically no effect on the clinical picture. This case had a generalized arthralgia and arthritis of one knee. Reference to Table V will show more details regarding this patient.

Case B13, with a slight gonococcal discharge and complicated by a peri-urethral abscess, did remarkably well but required a second course.

Cases B14 and B15 (B15 complicated by prostatitis), both persistent gonococcal urethritis cases, showed a clinical improvement at the end of the first course and an "apparent cure" at the end of the second.

Case B16 did not cease discharging immediately after the two uleron courses, but took a few days longer (three days after the cessation of the second course).

Case B17, showing toxic conjunctivitis, arthralgia, prostatitis, and gonococcal urethritis, did not respond well to three uleron courses (a uleron failure). This case later cleared up on other treatment and is now on T.O.C.

Case B18 required three uleron courses before an "apparent cure." Originally the urethral discharge contained diphtheroids and staphylococci in addition to gonococci.

Case B19 (prostatitis and unilateral epididymitis) showed only a slight improvement after one uleron course, but cleared up after the second, an "apparent cure" being noted nineteen days from beginning uleron.

Case B20 was a uleron failure. Before starting uleron a double epididymitis existed. The urethral discharge was slight. Gonococci were still demonstrable after three courses; indeed, after three courses the discharge became profuse. This patient is still on other anti-gonorrhoeal treatment (non-chemotherapeutic). This is the fifth uleron failure of this series of twenty cases.

Discussion and Conclusions

RESULTS IN ACUTE CASES

The analysis of 100 "early" cases leaves little doubt as to the value of uleron as a chemotherapeutic agent for acute gonorrhoea. It will have been observed that an interval was allowed before starting the first course and that irrigations were given in all cases. A number of acute cases were put on uleron at first attendance, but eventually I gave up this procedure as the results were less reassuring than those in this series. The belief expressed by Harrison, and some German authors, that a period should be allowed for the development of a natural resistance, was followed. The average duration of the urethral discharge before starting uleron treatment was, as already stated, almost three weeks (17.9 days). A preliminary investigation of cases treated by uleron alone (no irrigations) led me to think that for this series I should get better results by using irrigations from the first day of attendance at the clinic. Particular attention has been paid to the importance of a long observation period between "apparent cure" and application of the routine T.O.C. The T.O.C. must be as thorough for cases treated by chemotherapeutic methods as for cases treated by older methods.

The results obtained by uleron treatment in this series, although not 100 per cent., give good reason to believe that the drug has opened up a new era in the treatment of gonorrhoea. After one uleron course no fewer than 26 per cent. of the acute cases showed an "apparent cure" and were proved to be definitely "cured" at a later date. After two courses a further 35 per cent. gave a similar result, thus bringing the total up to 61 per cent. After three courses another 13 per cent. was added to the "apparent cures" (followed by successful T.O.C.), the total now reaching 74 per cent. One must admit that

relapses do occur after uleron treatment and also that some cases do not seem to respond to the drug at all. After one, two, or three uleron courses the relapses totalled 9 per cent. and the failures 17 per cent. One of the "relapses" appeared clinically free from gonorrhoea for a period of seven weeks before relapsing. I believe that there was no question in this case of re-exposure to infection.

Gonococcal complications before and after uleron treatment totalled 19 per cent. in this series, and in the control cases this was 24 per cent. The average duration of discharge (including the period before attending the clinic) for the "apparent uleron cures" was thirty-five days, in contrast to fifteen weeks in the control cases.

RESULTS IN CHRONIC CASES

Although it would not, in such a small series as twenty cases, be justifiable to give these results as percentages, one should be safe in concluding that uleron has an important place as a chemotherapeutic agent for such cases. All of the patients had had persistent discharge despite irrigations, and complications which had proved particularly resistant to routine treatment. As regards the actual results, Case B10, of sixteen weeks' duration, showed an "apparent cure" after one course. Twelve cases received two courses and were then "apparent uleron cures." Two (B16 and B18) responded more slowly, and five (B4, B5, B12, B17, and B20) were uleron failures. In this group, as with the series of 100 acute cases, one realizes that some gonococcal infections do not respond to uleron treatment in the least.

GENERAL POINTS

Complications due to uleron were few. Three patients complained of slight headaches during the uleron course, four of a slight nausea, and two developed a severe generalized urticaria (one after the second course and one after the third course). The generalized urticaria cleared up rapidly when the drug was stopped. Neither polyneuritis nor acute anaemia occurred in this series. My experience of sulphanilamide is limited to some fifty cases only, and the results were inferior to those from uleron. This does not agree with the findings of such authorities as Cockkinis and McElligott, but possibly I have been rather prejudiced against sulphanilamide, as I have found that large doses over a considerable period were necessary, which increased the possibility of drug reactions.

Uleron does not protect the patient against a fresh attack of gonorrhoea. Two cases in the first group were re-exposed to infection and the disease was just as acute as before. Both had been definitely cured and had passed tests, and there was thus no question of their being "relapses."

Finally, a word of warning is necessary against the indiscriminate and uncontrolled use of a drug such as uleron. If allowed to get into the hands of the patient who wishes to treat himself the results might be more disastrous than the disease itself.

Summary

1. Numerous references to the treatment of gonorrhoea by uleron have recently appeared in the medical literature; some of these are quoted. I wished to form an unbiased opinion of uleron and to add my findings to the British medical literature.

2. The drug has been used in two groups of patients:
 - (a) 100 cases of gonorrhoea treated at an early stage of

infection, and (b) twenty cases, resistant to the older methods of treatment, receiving uleron at a late stage of infection.

3. The first group, after a period of observation including test of cure, gave 74 per cent. cures, 17 per cent. failures, and 9 per cent. relapses. The second group gave five "failures" out of the twenty cases.

4. With the dosage used in this series (11 grammes per three-day course) no alarming drug reactions were observed. Three complained of slight headache, four of slight nausea, and two developed a generalized urticaria, which cleared up in about a week on cessation of the drug. No polyneuritis was encountered.

I have pleasure in expressing my thanks to Mr. A. E. Robertson, a member of my staff, for the valuable assistance rendered in the investigation of my cases.

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TREATMENT OF STERILITY

REPORT ON SIXTY-TWO CASES

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This investigation has been undertaken because on reviewing a series of forty-one cases which had been admitted to the gynaecological wards of the Royal Free Hospital for the treatment of sterility in 1936 it was found, on inquiry one year to eighteen months later, that only five (12 per cent.) had become pregnant. A dilatation, insufflation, and curettage was performed in each case, seventeen receiving in addition injections of hormones.

It was felt that these figures did not justify treatment in the wards and that perhaps similar results might be obtained if sterility cases were investigated and treated in the out-patient department. Between August 1, 1937, and May 31, 1938, sixty-two consecutive women who attended Miss Dearnley's out-patient department for sterility have been investigated and treated; forty-seven complained of absolute sterility, nine of one-child sterility, one that she could not become pregnant with a second husband (although she had had four children by the first husband, and the present husband had healthy spermatozoa as demonstrated by the seminal test), and five that they had had one or more miscarriages.

Routine Investigation of Sterility

A careful history was taken, and the duration of the marriage, the use or not of contraceptives, and any menstrual abnormality were noted. A routine Wassermann test was made, being found negative in every

instance. Nothing abnormal was detected on pelvic examination except retroversion in three cases, a unilateral hydrosalpinx in one case, and an undersized uterus in four cases. In each case the husband was asked to send a specimen of semen for examination, and thirty-nine of the sixty-two consented to this. Five (13 per cent.) showed no spermatozoa, and three (8 per cent.) very few and distorted specimens. Thus in 21 per cent. of the examined cases the husband was sterile. On account of the long distances many of the specimens had to be sent for examination no regard was paid to absence of motility provided the specimen was in all respects normal.

Uterosalpingography

Partly as a means of diagnosis regarding patency of the Fallopian tubes, and partly as a therapeutic agent, lipiodol was injected into the uterus. It was thought that this procedure might separate fine adhesions in a non-patent tube and that in view of the possible antiseptic action of the oil the endometrium would be left in a healthier state. No anaesthetic was given. The week following the end of the period was in most cases the time chosen to perform the test.

Technique

The patient was asked to lie in the dorsal position with the knees bent on a sterile towel on the x-ray table; a sterile bivalved speculum was then passed and the cervix painted with iodine. A uterine sound was employed to ascertain the direction of the uterine cavity; the two smallest-sized dilators were passed, so as to stretch the internal os gently if this was found tightly closed; and finally the insufflator (a modification of Provis's model with an oval plug, made for me by Messrs. Hawkins) was introduced. No vulsellum was used, but with the plug firmly pressed against the cervix 10 c.cm. of lipiodol was slowly injected and a radiograph taken.

It has been found that, provided the insufflator can be introduced past the internal os and the cervix is not unduly patulous, the lipiodol enters the fundus and passes into the tubes. Pain may be felt similar to that experienced during a retrograde pyelography, but not uncommonly there is no discomfort at all. In one case only of this series has there been any infection. This patient had a low temperature for a few days, and according to her private doctor she felt some pain, and there was tenderness in the pelvis on vaginal examination. Most of the patients attended twenty-four hours later for a second radiograph in order to demonstrate whether lipiodol had escaped through the Fallopian tubes into the pelvis. In twelve cases (19 per cent.) no lipiodol had entered the peritoneal cavity, suggesting absence of patency, and in two others it was doubtful whether there was a trace after twenty-four hours, but in both of these doubtful cases pregnancy occurred.

Since it is perhaps not generally agreed that one negative insufflation or lipiodol test should be accepted as conclusive evidence of occlusion of the Fallopian tube, the twelve negative cases (Table I) will be considered in further detail. In no instance where non-patency was demonstrated radiographically has the patient become pregnant. In one case the findings were confirmed at operation, and three cases were negative also to insufflation, but one of these, judging from the kymograph tracing, was rendered patent on one side by this procedure. Of the remainder, in two cases x-ray examination showed a unilateral hydrosalpinx, and in three there is a trace of lipiodol in one tube only; one of the latter had had a salpingectomy for tuberculous salpingitis two years