

# AMENORRHOEA: AN ANALYSIS OF CASES SEEN AT A GYNAECOLOGICAL ENDOCRINE CLINIC\*

BY

E. G. OASTLER, M.A., M.B., F.R.C.P., F.R.F.P.S.G.

AND

A. M. SUTHERLAND, M.D., F.R.F.P.S.G., F.R.C.O.G.

*From the Royal Samaritan Hospital for Women, Glasgow*

THE cases of amenorrhoea that are presented and analyzed are those that have been seen over the past six years at the Endocrine Clinic of a large and purely gynaecological hospital. Most of the patients attending the clinic were referred by other members of the staff, all of whom are gynaecologists. Thus the emphasis is on the gynaecological side, and the patients in the series to be described were referred primarily because of the amenorrhoea. As a result, the cases naturally tend to be selective, and it can be understood why certain types are so poorly represented. Thus few cases would be expected of amenorrhoea secondary to general systemic disease, such cases being sent to a general hospital; similarly, those cases associated with some gross endocrine disorder, such as Cushing's syndrome, diabetes and thyrotoxicosis, are also more usually sent to a general hospital, whether it be to an endocrine clinic or to the general medical out-patient clinic.

In the course of analyzing our cases of amenorrhoea the need for a comprehensive classification of this disorder soon became apparent. Although many papers have been written over the past twenty years on the subject of amenorrhoea, most of these deal each with a single aspect and make no attempt to present any classification. Classifications of amenorrhoea are infrequent, not only in papers on the subject but also in textbooks and monographs, both of gynaecology and of endocrinology. Those examples that we

have been able to find proved inadequate for our purpose, as so many of our cases were difficult to classify under existing headings. Further, there is considerable discrepancy and disagreement between various classifications, due largely to the differing particular interests of the workers concerned. It was thus necessary to devise a broad and general classification that would also include all the conditions encountered in our series and yet not be too detailed.

In planning the classification the usual broad separation into primary and secondary amenorrhoea was employed. The term primary amenorrhoea was applied to women of 18 years of age or over who had never menstruated. Secondary amenorrhoea was applied to women under the age of 40 who complained of amenorrhoea of at least 3-months duration, whether they had previously menstruated normally for some years or had only bled scantily and on a few occasions in their lives.

We suggest the following classification:

## PRIMARY AMENORRHOEA

### A. SEXUAL INFANTILISM

No sexual development and no secondary sex characteristics—by the age of 18 years.

#### (1) *Primary Pituitary*

Including: chromophobe adenoma, craniopharyngioma and asexual ateleiotic dwarfism; selective FSH deficiency; Fröhlich's syndrome (a hypothalamic lesion although it may be associated with a pituitary tumour).

#### (2) *Primary Ovarian*

Including ovarian agenesis and Turner's syndrome; disease of ovaries, such as tuberculosis and sepsis.

\* Based on a paper given to the Endocrine Club, Glasgow, on 10th December, 1954.

(3) *Other Endocrine Disorders*

Such as cretinism and juvenile myxoedema.

**B. SEXUAL HYPOPLASIA (HYPOGONADISM)**

With poor sexual development and slight secondary sex characteristics only—by the age of 18 years. (Often with short stature, and probably representing a degree of hypopituitarism; sometimes representing merely a delay in development.)

**C. ABSENCE OF MENARCHE**

With sexual development and secondary sex characteristics. ("Physiological" up to the age of 18 years.)

(1) *No Endometrial Development*

(a) With normal sized uterus which will respond to oestrogen.

(b) With hypoplastic uterus; but with little or no hypoplasia elsewhere.

(c) Disease of uterus but with normal uterine development; such as endometrial tuberculosis.

(d) With normal uterine development and no evidence of disease of uterus, but with no response to oestrogen: uterine insensitivity.

(2) *With Proliferative Endometrium*

Delay in onset of ovulation.

(3) *Psychogenic*

Fear, environmental change, etc. (probably acting through the hypothalamus and usually associated with anovulation).

(4) *Obesity (simple)*

May be associated with anovulation or with no endometrial development.

(5) *Cryptomenorrhoea*

Associated with a vaginal septum.

**D. WITH ABNORMAL SEXUAL DEVELOPMENT**

Hermaphroditism; pseudohermaphroditism (adrenogenital syndrome), and Cushing's syndrome.

**SECONDARY AMENORRHOEA**

In a woman, under 40, who comes complaining of amenorrhoea and who has had it for three months or more.

**A. GENERAL OR SYSTEMIC**

(1) Nutritional: starvation and anorexia nervosa. (The effect of these may be generalized or the action more specific through the pituitary with gonadotrophin deficiency.)

(2) Chronic infections, etc., such as tuberculosis, generalized or pulmonary; chronic nephritis, and malignancy.

(3) Intoxications, such as lead, alcohol and drugs.

**JOURNAL OF OBSTETRICS AND GYNAECOLOGY**

(4) Anaemia and other blood diseases.

(5) Other endocrine disorders: thyroid disorders (usually hyperthyroidism); diabetes; Addison's disease; adrenogenital syndrome; Cushing's syndrome.

**B. PSYCHOGENIC**

Fear, worry, sudden fright, etc. Change of climate or of environment. (Probably all anovulatory and acting through the hypothalamus.)

**C. OBESITY**

Usually associated with anovulation and a proliferative endometrium but may be associated with an inactive atrophic endometrium.

**D. PITUITARY**

Simmonds's disease, as in post-partum necrosis; tumour: including chromophobe and chromophil adenomata.

Persistent lactation:

(a) Chiari Frommel syndrome (always post-partum and associated with hyperinvolution of uterus).

(b) "Spontaneous" (may or may not be associated with a preceding pregnancy).

**E. PITUITARY-OVARIAN**

(1) Primary hypofunction—with poor sexual development in general (bleeding probably having occurred only scantily and on a few occasions).

(2) Secondary hypofunction ("ovarian failure")—with previous normal menstrual history.

(3) Anovulation (with a proliferative endometrium).

**F. OVARIAN**

Disease (destructive):

(a) Infection, such as tuberculosis and sepsis.

(b) Tumour, such as Krukenberg's tumour.

Stein-Leventhal syndrome with bilateral cystic ovaries. Arrhenoblastoma.

Removal by surgery; destruction by irradiation.

**G. UTERINE**

Disease: endometrial tuberculosis; puerperal sepsis. Destruction as a result of a previous curettage. Insensitivity. Cryptomenorrhoea (due to cervical stenosis). (Hysterectomy.)

**H. PREGNANCY AND PHYSIOLOGICAL LACTATION****I. PREMATURE MENOPAUSE**

Distinguishable from secondary hypofunction (ovarian failure) by the presence of menopausal symptoms.

**PRIMARY AMENORRHOEA**

Some comments are desirable with regard to certain points in the classification. The age of 18 was chosen as the earliest for accepting the definition of primary amenorrhoea, in order to

eliminate as far as possible cases merely of slight delay in development. This applies particularly to those cases showing the less severe defects, such as would be included under the category of sexual hypoplasia or of absence of menarche. There is also the difficulty before a certain age of classifying a case as one of sexual infantilism, since it may later fall into the less severe category of sexual hypoplasia; but by the age of 18 this is much less likely to occur.

The term asexual ateleiotic dwarfism is applied to the so-called pituitary dwarf, a diminutive person with normal proportions, with no secondary sexual development and with low urinary FSH excretion. The aetiology of this condition is usually difficult to determine; some cases are associated with nutritional defect, such as coeliac disease, and others appear to be congenital and probably due to some primary pituitary defect. Selective FSH deficiency represents sexual infantilism without dwarfism; the cases are usually rather tall with typical eunuchoid proportions and are differentiated from the similar picture of eunuchoidism due to primary ovarian defect by low urinary FSH excretion. The patients with sexual infantilism due to primary ovarian causes may either be short or tall in stature, the latter with typical eunuchoid proportions. The former are examples of ovarian agenesis, the stunting of growth being genetic, and in both examples the urinary FSH excretion is raised.

With regard to the second group, that of "Sexual Hypoplasia", it was obvious as soon as we came to analyze our own series that there was a considerable number of patients who were certainly not cases of sexual infantilism and yet were more than cases merely showing a hypoplastic uterus. They appear to lie between these two groups, indicating varying degrees of hypogonadism. All our cases were rather short in stature, with normal proportions; and in all the cases where urinary FSH was estimated this was found to be low. These facts suggested a degree of hypopituitarism and we looked upon this group as probably representing delayed development due to hypopituitarism, some of whom would probably develop all right, as in fact did occur in some of the cases in our series, while others might remain deficient all their lives.

The cases classified under the heading "Absence of Menarche" represent the best developed of the first three groups, all patients having normal or nearly normal female figures. Those with a proliferative endometrium are the nearest to normal, representing anovulation and probably merely a delay in the onset of ovulation. Those showing no endometrial development are stages in hypoplasia, probably representing an inequality in response; thus some girls start to menstruate very early while their breasts are still small and undeveloped, whereas others may have extremely well-developed breasts but have a hypoplastic uterus and menstruation may not start for a few years.

Investigation of patients with primary amenorrhoea always included a thorough medical examination for evidence of general systemic disease as well as for evidence of other endocrine disorders. Careful measurements were taken to determine body proportions. X-rays of skull and of long bones for epiphyseal development were done routinely. An examination under anaesthesia was usually advised—except in certain cases of group C (absence of menarche)—where there was reason to expect merely a delay in or absence of ovulation. In those cases chorionic gonadotrophin was given, 1,500 International Units by injection daily for 5 consecutive days. If there was no bleeding after these injections or where curettage was carried out and no endometrium was obtained, an "artificial period" was usually given, the details being as follows: on the 1st, 3rd, 5th, 8th, 10th, 12th, 15th, 17th and 19th days Oestradiol Benzoate, 50,000 International Units was given by injection. With the 8th injection, 10 mg. progesterone was given. With the 9th injection, and on the five consecutive days following the 9th injection, 15 mg. progesterone was given.

Out of a total of 176 cases of amenorrhoea there were 30 patients with primary amenorrhoea. The cases were made up as follows:

*Sexual Infantilism:* 6 cases

*Primary Pituitary:* 4 cases: Chromophobe adenoma (1); Ateleiotic or pituitary dwarf (1); Selective FSH deficiency (2).

*Primary Ovarian:* 2 cases: "Idiopathic" (? ovarian agenesis) (1); Tuberculous salpingo-oöphoritis (1).

*Sexual Hypoplasia* (hypogonadism): 11 cases

*Absence of Menarche:* 12 cases

*With no endometrial development:* 9 cases: With normal sized uterus (1); With hypoplastic uterus (5); With normal sized but insensitive uterus (3).

*With proliferative endometrium:* 2 cases.

*Obesity* (simple): 1 case.

*Abnormal Sexual Development:* 1 case.

*Virilism* (adrenogenital syndrome).

The patient with the chromophobe adenoma was a girl of 19, slightly undersized and with no secondary sexual development. She has developed well with replacement therapy which has included oestrogen implants. Surgery is now being considered because of commencing visual field defect. The case of ateleiotic or pituitary dwarfism was a small, elf-like child of 21 years of age who is still being treated with small doses of thyroid only, in the hope that further growth will occur. The exact aetiology of her condition has not been established. The 2 cases of selective FSH deficiency were tall, thin girls of 26 and 29 years of age respectively, with typical eunuchoid figures and no secondary sexual development. In both cases the FSH excretion was less than 20 mouse units/diem. These 2 patients have received replacement therapy with oestrogen implants and now show good secondary sexual development. One of the two cases of sexual infantilism due to primary ovarian causes had genital tuberculosis. She had a typical eunuchoid figure but her FSH excretion was low, less than 20 mouse units/diem, which might be explained by her tuberculous infection. The other case was a girl of 19 years of age with normal stature and proportions, but with no secondary sexual development. She had had hot flushes for 3 years and her urinary FSH excretion was 60 mouse units/diem. It was considered that she probably had an unexplained developmental defect of the ovaries.

The 11 cases of sexual hypoplasia (hypogonadism) ranged in ages from 18 to 22 years. They were all short statured, 5 being under 4 feet 10 inches in height, but all 11 had normal proportions. In all the cases where FSH was estimated (5 patients), it was found to be low, less than 20 mouse units/diem. There were 5 cases exceeding 5 feet in height and in all of these treatment was directed to their genital development only. Three of these cases were found to be sensitive to oestrogen, one of whom started to bleed cyclically on her own after responding to an "artificial period". Two of the cases were found to be insensitive to oestrogen. Of the 6 cases under 5 feet, one was given oestrogen implants on two occasions and within 2 years was bleeding cyclically on her own. One was given thyroid in small dosage and one implant of oestrogen. There was good effect both of growth and of sexual development, but no bleeding has yet occurred. Four cases were given thyroid only since it was considered that growth in stature was the more important factor. In 2 cases there was very considerable improvement both in growth and development but no bleeding has yet occurred in either. One case is too recent yet to assess, the other has shown little or no improvement.

Among the 12 cases with absence of menarche the one patient with no endometrial development, but with a normal-sized uterus, bled satisfactorily after an "artificial period": she was later found to have a dysgerminoma. Of the 5 patients with hypoplastic uteri, 2 had "artificial periods" and not only bled satisfactorily after these but continued to bleed cyclically on their own thereafter; 2 others also received "artificial periods", one of whom bled satisfactorily after each of three, but did not bleed on her own. The other did not bleed even after three courses of injections. The fifth patient was given an implant of oestrogen but it is too early to assess the effect of this. Of the 3 patients with normal-sized but insensitive uteri, none bled after three or more "artificial periods" and endometrial biopsies repeated after the courses of injections still showed no endometrial response.

Both the cases with a proliferative endometrium bled after injections of chorionic gonadotrophin, one continuing to do so

cyclically on her own thereafter. The case of obesity did not have an endometrial biopsy performed, but she bled satisfactorily after an "artificial period". Weight reduction was also advised but she subsequently defaulted. The case of virilism was a girl of 20 years of age of very small stature and with no secondary sex development and gross facial and body hirsutism. She had had gross clitoral enlargement, but this organ had been amputated before she was seen at the clinic. 17-ketosteroid excretion was very high, and bilateral adrenal hyperplasia had previously been confirmed at laparotomy. This patient has shown considerable breast development and has bled vaginally, continuing to do so fairly regularly since commencement of cortisone therapy.

#### SECONDARY AMENORRHOEA

Out of the total of 176 cases of amenorrhoea in the present series, 146 were of secondary type. The cases in this group were made up as follows:

Pituitary-ovarian hypofunction ..	87 cases
Obesity .. .. .	29 cases
Anovulation .. .. .	8 cases
Galactorrhoea .. .. .	5 cases
Endometrial tuberculosis .. .. .	4 cases
Psychogenic causes .. .. .	4 cases
Pituitary necrosis .. .. .	2 cases
General or systemic conditions .. .. .	2 cases
Destruction of ovarian function .. .. .	2 cases
Insensitive uterus .. .. .	1 case
Disease of uterus .. .. .	1 case
Premature menopause .. .. .	1 case

The initial investigation of these cases of secondary amenorrhoea consisted of a thorough general examination, particular attention being paid to the exclusion of endocrine conditions. Where feasible, pelvic examination and endometrial biopsy were also carried out at the Endocrine Clinic, but in quite a number of cases this was not possible, as many of the patients were young, unmarried girls. In such cases, where endometrial biopsy was later judged necessary, admission to hospital was arranged and the procedure was carried out under general anaesthesia. The subsequent management varied with the condition present, and reference will now be made to each of these categories in turn.

#### (1) *Pituitary-ovarian Hypofunction*

In analyzing the cases of secondary amenorrhoea, it was seen that by far the largest number seemed to be examples of varying degrees of sexual hypofunction. But it was difficult to determine whether the primary defect was in the pituitary or the ovary. For this reason the term "Pituitary-ovarian Hypofunction" was used to describe this group. The 87 cases can conveniently be divided into primary and secondary types.

(a) *Primary hypofunction*: 34 cases. The patients in this group had never had a normal menstrual cycle. Menstruation was at best scanty and infrequent, and, in some of the more marked cases, only a few periods had occurred over a number of years. On pelvic examination, the uterus was invariably found to be small, and general sexual development was usually poor. Endometrial biopsy was carried out in 21 of these patients, with the following results:

No tissue obtained .. .. .	12 cases
Inactive proliferative endometrium .. .. .	4 cases
Atrophic endometrium .. .. .	2 cases
Cystic glandular hyperplasia .. .. .	1 case
Irregular ripening of endometrium .. .. .	1 case
Secretory phase of cycle .. .. .	1 case

The initial treatment consisted of either an "artificial period" or of chorionic gonadotrophin, depending on the circumstances of the individual case. Subsequent management depended on the initial response to these measures. The results can be grouped as follows:

Bled after some form of artificial period .. .. .	11 cases
Bled after chorionic gonadotrophin .. .. .	3 cases
Failed to bleed after chorionic gonadotrophin, bled after artificial period .. .. .	5 cases
Failed to bleed after chorionic gonadotrophin, bled after endometrial biopsy .. .. .	1 case
Bled after endometrial biopsy only .. .. .	1 case



Failed to bleed after chorionic gonadotrophin, then defaulted .. .. . 3 cases

No result. Defaulted or too early in follow-up .. .. . 10 cases

It will be seen that at least one menstrual period occurred in all patients who continued to attend for any length of time. Although the number of defaulters was large, 3 of the relatively small number who attended regularly continued to menstruate without further treatment.

(b) *Secondary hypofunction*: 53 cases. All the patients in this category had had normal menstrual periods for at least a few consecutive months, and in many cases for a number of years. In every instance the uterus was found to be small, and general sexual development was frequently though not invariably poor. Endometrial biopsy was carried out in 38 of these patients, with the following findings:

No tissue obtained .. .. . 21 cases

Atrophic endometrium .. .. . 8 cases

Inactive proliferative endometrium .. .. . 6 cases

Secretory endometrium .. .. . 2 cases

Cystic glandular hyperplasia .. .. . 1 case

The initial treatment was on similar lines to the primary hypofunction group, an "artificial period" or chorionic gonadotrophin being given according to the circumstances of the individual case. Subsequent management depended on various factors, including the response to the initial measures. The results can be grouped as follows:

Bled after some form of artificial period .. .. . 19 cases

Bled after chorionic gonadotrophin .. .. . 1 case

Failed to bleed after chorionic gonadotrophin, bled after artificial period .. .. . 6 cases

Bled after endometrial biopsy only .. .. . 4 cases

Bled spontaneously without treatment .. .. . 3 cases

Failed to bleed after chorionic gonadotrophin, then defaulted .. .. . 4 cases

No result. Defaulted or too early in follow-up .. .. . 16 cases

It will thus be seen that every patient in this group who attended for any length of time bled at least once. Again the number of defaulters was large, but, of the relatively small group who continued to attend for a reasonable length of time, 4 continued to bleed regularly, and one later became pregnant. The patients who reported return of normal menstruation before treatment was started are excluded from this group.

## (2) *Obesity*

There were 29 cases of obesity associated with amenorrhoea. In some of these the obesity was only of short duration, but frequently it had been present for some years. The increase in weight sometimes came on after pregnancy. In other cases there was no apparent reason, and several patients said that it followed marriage. The duration of the amenorrhoea varied from 3 months to 4 years. Endometrial biopsy was carried out in 12 cases in this group, 7 showing an atrophic endometrium and 5 an inactive proliferative endometrium of anovulatory type. Weight reduction was advised in all cases, the patient usually being put on an 800 calory diet, frequently with Dexedrine in addition. In a few instances, use was also made of chorionic gonadotrophin or of "artificial periods". The results in the obesity group can be divided into 4 categories:

(a) Very successful. 12 cases. Following weight reduction, the menstrual periods returned and the patients subsequently had what appeared to be normal regular cycles. Three of these patients later became pregnant, 2 after more than 6-months amenorrhoea. Eight of these patients had dieting only, 2 had diet and chorionic gonadotrophin, and 2 had diet and "artificial periods".

(b) Temporary success. 3 cases. Bleeding did occur after weight reduction, but a normal cycle was not restored.

(c) Unsuccessful. 2 cases. Weight reduction was satisfactory, but bleeding did not return.

(d) No result. 12 cases. Most of these patients defaulted, but in a few it is as yet too early to assess the result.

It will be seen from these figures that the type of secondary amenorrhoea associated with abnormal gain in weight offers a much better prospect of cure than the type associated with genital hypofunction.

### (3) *Anovulation*

Eight cases. The patients in this group had ceased to ovulate, but could usually be stimulated by chorionic gonadotrophin to bleed. Five of the 8 patients had an endometrial biopsy, all showing an inactive proliferative endometrium. All 5 were given chorionic gonadotrophin, 4 bleeding thereafter; the fifth patient showed a well-developed proliferative endometrium before chorionic gonadotrophin but did not bleed. Three of these 5 patients continued to bleed cyclically on their own and one defaulted. The other 3 did not have an endometrial biopsy, but all bled after chorionic gonadotrophin, 2 continuing to do so and one defaulting.

### (4) *Galactorrhoea*

Five cases. All the patients in this group were married, parous women, and all 5 showed some degree of obesity and gave a history of gain in weight. In 3 of these the amenorrhoea persisted after the birth of a child. In each instance the uterus was small for a parous woman, the length of the cavity being  $2\frac{1}{2}$  inches, but it is doubtful if they are true examples of the Chiari-Frommel syndrome. In one further case the uterus was of normal size and the fifth patient was found to have a chromophobe adenoma of the pituitary. In all 5 cases an "artificial period" was given and bleeding followed. The chromophobe adenoma was removed successfully, but in this, as in the other 4 cases, the galactorrhoea persisted in spite of various forms of treatment. These results are in keeping with the present view that there is no curative treatment for this interesting condition.

### (5) *Tuberculosis of the Endometrium*

There were 4 patients with endometrial tuberculosis, 2 being unmarried. There was no history of previous pregnancy in any case. Although we do not, as a routine measure, carry out endometrial biopsy in every unmarried girl with amenorrhoea, we feel that it is necessary

to do so where chorionic gonadotrophin has produced no bleeding, particularly where the secondary sex characters are well developed and there is nothing to suggest hypofunction. Failure to carry out this procedure in such cases will involve the risk of missing occasional examples of endometrial tuberculosis. All 4 patients have since been included in a large scale investigation into various aspects of genital tuberculosis in women. Each has received a course of streptomycin and PAS and subsequent endometrial biopsies have shown that the tuberculous infection has not recurred. An interesting feature of this group is that normal menstruation was restored in all 4 patients following treatment of the tuberculous condition.

### (6) *Psychogenic Causes*

There were 4 patients in this group, aged from 18 to 26 years. In one case the amenorrhoea dated from a fall, in 2 others from a fall from a bicycle, and in the fourth case from seeing a sister fall from a bicycle. This association with bicycles is interesting, but the number of cases is too small to enable us to draw any conclusions. Two of these patients showed proliferative endometrium on biopsy; both bled after an "artificial period", and both later developed cystic glandular hyperplasia. The other 2 had atrophic endometrium on biopsy; one bled after an "artificial period" and continued to bleed normally without further treatment, the other bled only after an "artificial period".

### (7) *Pituitary Necrosis*

There were 2 patients in this group, one with typical Simmonds's disease who had had amenorrhoea for 4 years, the other with Simmonds's disease and diabetes insipidus.

### (8) *General or Systemic Conditions*

In this group there was one case of Felty's syndrome, a form of rheumatoid arthritis, and one case of hyperthyroidism. Both patients were referred to a general hospital for medical treatment.

### (9) *Destruction of Ovarian Function*

Two cases. One patient had amenorrhoea following previous removal of both tubes and

ovaries for pelvic tuberculosis. The other had amenorrhoea following deep X-ray therapy for Hodgkin's disease. Both patients complained of hot flushes.

#### (10) *Insensitive Uterus*

There was only one example of insensitive uterus in the whole series. This patient was aged 23 years and complained of amenorrhoea of 18-months duration. No tissue was obtained on endometrial biopsy. Three "artificial periods" were given without result and a second endometrial biopsy also failed to produce any tissue. This patient was not obese.

#### (11) *Disease of Uterus*

The one patient in this category complained of amenorrhoea of 17-months duration, following a septic abortion. No tissue was obtained on endometrial biopsy and there was no bleeding after an "artificial period". It seems probable that the amenorrhoea in this case is permanent.

#### (12) *Premature Menopause*

The only patient in this category had amenor-

rhoea with well-marked menopausal symptoms. Bleeding occurred following both chorionic gonadotrophin and "artificial periods", but the menopausal symptoms persisted and the periods did not recur. She was aged 35 years and had had amenorrhoea for 10 months.

#### CONCLUSIONS

Some writers have questioned the advisability of treating patients with amenorrhoea. It is considered, however, that the results obtained in the present series amply justify the measures employed. In spite of the fact that a large number of patients defaulted in the early stages, bleeding was induced by one or other form of treatment in most cases, and menstruation was re-established on an apparently normal basis in a substantial number. The psychological effect of restoration of bleeding, even temporarily, has been most beneficial and, in a few cases, the subsequent occurrence of pregnancy is proof of restoration of normal function. In addition, this investigation has brought to light a number of conditions requiring general medical or surgical treatment, such as endometrial tuberculosis.