REPORT OF AN ENDOCRINE CLINIC

BY

B. JOAN HARAM, M.R.C.S., L.R.C.P.*Assistant Pathologist, Elizabeth Garrett Anderson Hospital*

An endocrine clinic in the charge of Miss Landau was inaugurated at the Elizabeth Garrett Anderson Hospital in February, 1938, and it is possible that a record of the results obtained after a year's work may be of some interest in view of the recent widespread increase in the use of endocrine therapy. The organization of such a clinic presented many difficulties, and as a result of the experience gained various alterations and improvements have suggested themselves.

The clinic was held weekly, and patients were referred to it from other departments of the hospital or sent direct by their own doctors. Unfortunately, from the point of view of a subsequent estimation of results, a number of them had had previous endocrine treatment. Altogether 208 patients attended, but some of these were found to be unsuitable, so were transferred to other clinics, some were sent back to their private doctors, and some attended too late in the year for the effect of their treatment to be apparent. Of the remainder many did not attend regularly on account of the lack of funds or time, and some were disheartened after perhaps one course of injections. Sixty-six who failed to return in due course or to report progress were communicated with during the year, but only fifty replied, from which it will be seen that the assessment of the results obtained has been complicated by many extraneous circumstances. In consequence seventy-seven cases out of the total number can be disregarded, leaving 131 who received treatment over a reasonable period of time. In the following analysis, however, every patient who attended at all is taken into consideration. The numbers in each group and the subsequent results will be found in the accompanying table.

Analysis of Results

Condition	Total Number	Number Dis-counted	Reduced Total	Success	Improvement	
					Much	Slight
Amenorrhoea	25	7	18	2	1	4
Oligomenorrhoea ..	35	12	23	9	6	5
Menorrhagia	37	16	21	8	11	0
Dysmenorrhoea .. .	7	0	7	1	0	0
Menopausal symptoms	14	4	10	8	0	1
Sterility, with						
(a) Regular cycle ..	21	5	16	1	—	—
(b) Menorrhagia .. .	5	0	5	1	3	—
(c) Oligomenorrhoea ..	22	8	14	2	6	—
(d) Amenorrhoea .. .	10	4	6	0	3	2
Unclassified	20	9	11	2	2	0
Unsuitable cases ..	12	12	0			
Totals	208	77	131	34	32	12

The principal disorders dealt with were amenorrhoea, oligomenorrhoea, menorrhagia, dysmenorrhoea, menopausal symptoms, and sterility. There were also twenty cases which were unclassified and twelve which were found to be unsuitable for treatment at the clinic.

Amenorrhoea

By this we implied the absence of menstruation for six months or longer. Twenty-five such cases attended during the year, of which one was primary and twenty-four secondary in type. The duration of the amenorrhoea extended from seven months to six years, the majority being over a year. Twenty-three of the patients were single and two married.

The primary case had a history of tuberculous peritonitis, for which she had been operated upon in 1916. Her general

health was good, and she was advised to have no endocrine treatment.

In the secondary group seven can be disregarded for the various reasons enumerated above. One of these was found to have pulmonary tuberculosis, and was admitted to hospital. Of the remaining seventeen, two cases responded with four regular periods following nine and twelve months' amenorrhoea respectively, one being treated with thyroid only and the other with courses of dimenformon and antuitrin-S. A somewhat similar case had four irregular periods after dimenformon only, and another menstruated regularly for a few months after thyroid and iron, but subsequently relapsed. Seven cases had one period following prolonged amenorrhoea, but in two of these the bleeding was probably due to oestrin withdrawal, and in the remaining five it is unlikely that a regular cycle has been established. Four cases had only had one or two periods since puberty, and although none of them menstruated, two improved in general health, one with theelin and one with antuitrin-S. The remaining two did not continue treatment. Two cases failed entirely to respond, in spite of treatment for four months or longer.

Oligomenorrhoea

In this group fourteen patients were married and twenty-one single. Of the total thirty-five cases twelve may be disregarded. On oestrin preparations, antuitrin-S, thyroid, and iron nine cases showed a sustained improvement in the regularity and amount of flow, six a certain amount of improvement, and five a temporary response only. Two became better in their general health and one was unaffected by four months' intensive treatment.

Menorrhagia

Thirty-seven patients complaining of menorrhagia attended during the year, sixteen being married and twenty-one single. Of the total number sixteen may be discounted. One of these was found to have a cough and was admitted to hospital, a radiograph showing a recent phthisical lesion. Of the remaining twenty-one cases eight had several normal periods (from three to nine in number) after treatment with proluton (five cases), mepformon (one case), and iron (two cases). Three of the cases treated with proluton have had normal and regular periods for five, seven, and eight months respectively since the cessation of the treatment. Eleven cases showed some improvement, including two cases of puberty menorrhagia, and two failed to respond after five or six months' endocrine therapy.

Dysmenorrhoea

Very few cases of dysmenorrhoea were referred to the clinic, the majority being dealt with successfully in other departments of the hospital. Of the seven who did attend only one showed definite improvement after dimenformon, the remaining six being either unaffected by endocrine therapy or responding equally well to the psychological effect of a course of injections of inert sterile olive oil.

Menopausal Symptoms

These patients, who complained principally of flushes and headaches, proved to be the most responsive to treatment. Four of the fourteen who attended can be disregarded; seven showed a great improvement when treated with menformon or theelol by mouth, and a further successful result was that of a girl of 22 who had had a bilateral salpingo-oophorectomy for old-standing tubercle, and who was treated two months later by the implantation of a 15-mg. tablet of oestrone beneath the skin of the abdominal wall. Deanesly and Parkes (1937) and Parkes (1938) describe the advantage of the slow rate of absorption obtained by this method, and Bishop (1938) records a very similar case. The flushes decreased from two to one daily, and have now, after six months, ceased to trouble the patient at all. The economic advantage to the patient and the hospital is obvious, and it is hoped that further opportunities for proving the value of this method of treatment will occur. The two remaining cases in this group improved at first but relapsed later in spite of continued treatment.

Sterility

The fifty-eight cases of sterility were divided into two groups—those with a regular cycle (twenty-one cases) and those with an irregular cycle (thirty-seven). Of the latter, five complained of menorrhagia, twenty-two of oligomenorrhoea, and ten of amenorrhoea. In most cases the patency of the Fallopian tubes had been tested by uterosalpingography, and the activity of the husband's semen established before endocrine therapy was initiated. It was not, however, always possible to achieve this. It is interesting to note that Moore White (1939) also reports this difficulty as regards the husbands, and the rate of male sterility in her examined cases is 21 per cent. This high result emphasizes the importance of this investigation in all cases.

Sterility with Normal Cycle.—Five of these twenty-one cases may be disregarded; three became pregnant, but in only one case, a patient who had been married for two and a half years, was the pregnancy presumably due to endocrine treatment. The method adopted in this and the majority of these patients was on the same lines as that originally laid down by Kaufmann (1934) for promoting a normal cycle in castrates. Dimenformon, 10,000 I.B.U., was injected on the fifth day of the cycle, followed by 50,000 units on the twelfth day and proluton, 1 or 2 mg. daily, from the twenty-second to the twenty-sixth day inclusive. In three cases the chance of pregnancy was remote, two of these patients being shown by uterosalpingography to have a uterus bicornis (and the husband of one of these was reported sterile on a single examination of the semen), and the third being a patient aged 42 who had been married for eighteen years. Pelvic abnormalities were found in four cases, and in the remaining six no adequate reason has as yet been discovered to account for the failure to become pregnant. It is interesting to note that in two of these the regularity of the menstrual cycle was disturbed by hormonal administration.

Sterility with Menorrhagia.—Of the five cases accompanied by menorrhagia one patient became pregnant after intensive endocrine treatment, three were improved as regards the menorrhagia, and one was unaffected.

Sterility with Oligomenorrhoea.—Out of twenty-two cases eight may be disregarded. Three patients became pregnant, two presumably as a result of hormonal treatment, one of whom had been married for three and a half years and one for six years. Six showed improvement in the regularity of the cycle, and in three cases the condition remained unchanged. The other two cases had complicating conditions—one a history of tubal abortion, the remaining ovary being tender and prolapsed, the other having recently had a suprasellar cyst removed with apparently complete recovery.

Sterility with Amenorrhoea.—Out of ten cases four may be discounted, three had one or two periods after treatment and felt better in general health, two improved generally but failed to menstruate, and one was unaffected.

Unclassified Conditions

Of the twenty cases nine may be disregarded. The remaining eleven comprised two pregnant patients with histories of previous miscarriages, one case each of dyspareunia, relative sterility, frigidity, leucoplakia, leucorrhoea, and macromastia, and three cases of pruritus vulvae. One of the pregnant patients was treated with antuitrin-S, 1 c.cm. weekly for five months, and was delivered normally at term; the other was treated with progesterin, 1 c.cm. weekly for three months, and is now nearly six months pregnant and has shown no sign of miscarriage. The patient who complained of dyspareunia improved with a course of gonadyl, and the case of leucorrhoea responded to dimenformon. The remainder failed to respond to endocrine therapy.

Investigations

As an indication of the existing condition and a guide to treatment endometrial biopsies were performed in the clinic upon twenty-eight patients, care being taken, when possible, to ensure that no endocrine treatment had been

given previously and that the secretory phase in the cycle had been reached, in order that any luteal deficiency might be detected. Two of the patients complained of oligomenorrhoea, twelve of menorrhagia, one of dysmenorrhoea, two of sterility with a regular cycle, five of sterility with menorrhagia, and six of sterility with oligomenorrhoea.

On histological examination both cases of oligomenorrhoea and the case of dysmenorrhoea showed a delay in the development of the luteal phase. Ten cases of menorrhagia showed the appearances expected for the time in the cycle at which the biopsy had been performed, and the other two showed luteal deficiency, one in a very considerable degree. Both these responded to proluton, the severe case needing intensive treatment. It is interesting to note that in none of this series was there evidence of metropathia haemorrhagica.

The two cases of sterility with a normal cycle revealed a normal endometrium. Of the cases of sterility accompanied by menorrhagia two showed the secretory phase as expected and one subsequently became pregnant, one showed great variation, and two suggested luteal deficiency. Of the patients complaining of sterility and oligomenorrhoea, all six showed the appearance characteristic of an earlier phase in the cycle than the date of the last period suggested, this delay being very marked in five cases.

In view of the fact that great variation in appearance may occur in the different fragments of a complete curettage it is probable that too much importance may be attached to the interpretation of a single small strip. Wollner (1937, 1938), in his description of cervical biopsies, while stressing their advantages also emphasizes the scarcity of patients with a normal endometrium or cervical mucous membrane. Nevertheless, the similar histological appearances found in all the cases of sterility accompanied by oligomenorrhoea are worthy of note, and must surely be more than coincidental. In five cases which suggested the possible presence of excess folliculin—four of them complaining of menorrhagia and one of oligomenorrhoea—the hormonal content of the urine was estimated by Professor Crew, but in each instance the amount of oestrone excreted was much below the normal level.

In twenty-three cases vaginal smears were examined, but as unfortunately only a few of these were repeated after treatment and they showed no appreciable improvement no deductions can be drawn from the results obtained.

Discussion and Conclusions

From the above table it will be seen that after a year's work only thirty-four unqualified successes, thirty-two considerable improvements, and twelve slight responses can be reported out of a total of 131 cases—on the face of it a disappointing result, which is recorded with no feeling of achievement but as an illustration of the problems which arise when conducting such a clinic.

For an accurate assessment of results it is essential that standardized routine methods of investigation should be employed for each pathological condition, and, if possible, one clinician should deal entirely with one such group. Preferably each patient should be treated throughout by the same clinician, and one line of treatment only should be followed. In the present instance the clinic grew more rapidly than was expected, and cases were sometimes dealt with individually rather than with reference to the ultimate correlation of results. In consequence a certain amount of the experimental value of the work was lost. It is obviously desirable to accept only those patients who are prepared to undergo a long and expensive course of treatment, who have had no previous endocrine therapy, and in whom, therefore, the issue is clear. On considering the amount of time involved and the expense incurred by a patient undergoing perhaps several courses of injections, it is unlikely that a high percentage of successful

results will ever be achieved with this mode of treatment, and it is indeed questionable whether it is worth while attempting to treat upon these lines cases of amenorrhoea and oligomenorrhoea in which the general health is otherwise excellent.

If the absolute efficiency of oral administration could be established many problems of hormonal therapy would obviously be solved, especially in hospital practice. Much is claimed for the synthetic preparation stilboestrol, and its recent introduction into the clinic encourages the hope of more satisfactory results in future.

Summary

A year's work in a newly established endocrine clinic is described, and reference is made to the difficulties encountered in the estimation of results.

A detailed analysis is given of the conditions treated.

The results are discussed, and various improvements in organization are considered.

My thanks are due to Miss Landau, F.R.C.S., for permission to report the work of the clinic, to Dr. A. N. Macbeth for her advice and help, and to the firms of Organon, Schering, Parke Davis, British Drug Houses, Roussel, and Paines and Byrne for their generous supplies of various endocrine preparations.

REFERENCES

- Bishop, P. M. F. (1938). *British Medical Journal*, 1, 939.
Deanesly, R., and Parkes, A. S. (1937). *Proc. roy. Soc.*, B, 124, 279.
Kaufmann, C. (1934). *Proc. roy. Soc. Med.*, 27, 849.
Parkes, A. S. (1938). *British Medical Journal*, 1, 371.
White, M. Moore (1939). *Ibid.*, 1, 62.
Wollner, A. (1937). *Surg. Gynec. Obstet.*, 64, 758.
— (1938). *Amer. J. Obstet. Gynec.*, 36, 10.

Nova et Vetera

AN EIGHTEENTH CENTURY SMALL-POX HOSPITAL

The detailed account given below of the administration and working of the first small-pox hospital in England, and apparently in Europe, occurs, rather surprisingly, in the anonymous topographical work *London and its Environs Described*, which was published in 1761. The hospital was then situated in "Cold-bath Fields," Clerkenwell, with a subsidiary building in Lower Street, Islington.

According to Woodville (1796)* the institution called the "Middlesex County Hospital for Small-pox" had begun in 1746, as a house with beds for thirteen patients, in Windmill Street, Tottenham Court Road; and it had undergone several changes of site before the governors in 1752 purchased the "spacious building in Cold-bath Fields." The frequent moves of the charity during its first six years were due not only to the governors' desire for greater and better accommodation for infected patients and cases for inoculation, but also to the not unnatural distaste of the residents in each locality for having a small-pox hospital as a near neighbour. In at least one instance (in the Cavendish Square area) local opposition had caused the project of transferring the hospital to larger quarters to be abandoned after the new house intended for the purpose had already been purchased and equipped; while the transfer to Cold-bath Fields was actually the subject of litigation, by "the church-wardens and overseers of the poor" of the parish of St. James's, Clerkenwell, who unsuccessfully moved the Court of Chancery for an injunction to restrain the governors from receiving any infected patients at the hospital.

The building in Cold-bath Fields is briefly described in the topographical work as follows: it "is a very plain

neat structure. The centre, which projects a little from the rest of the building, is terminated on the top by an angular pediment, on the apex of which is placed a vase upon a small pediment." Woodville states that the building contained six wards and 130 beds. The first presidents of the charity were the Duke of Marlborough and the Bishop of Worcester; the first physician in charge of the patients was Dr. Robert Poole, who was succeeded by Dr. Archer in 1748; the first secretary was Mr. Wm. Umfreville, Attorney. Woodville himself became physician to the hospital in 1791.

The account of the charity given in the topographical work is quoted from "the report published by the governors," evidently in 1759-60. This, as will be seen, includes not merely a discussion of its history and operation, but also a spirited defence of the practice and results of inoculation against small-pox, as then applied, with a tactful reproof to the already active opponents of this type of preventive medicine. It may be recalled that inoculation against small-pox, by the method of "variolaion," had been introduced to England in 1721 through the energetic propaganda of Lady Mary Wortley Montagu, who had her daughter inoculated in London that year, having had her son so treated in Constantinople some years earlier. Variolation by more or less primitive means had, however, been practised in the East from time immemorial, and Creighton (1894)† gives an interesting account of its use as a "folk-lore" method of protection against small-pox in parts of Wales and Scotland, long before it was formally introduced to the medical profession in London. As practised in England in the eighteenth century, it was a closely similar clinical procedure to vaccination, but, since vesicle fluid or crust material from an actual, though mild, case of human small-pox was used to inoculate the subject, he developed the disease itself, usually in a comparatively slight, or "varioid," form. Sometimes, when the infective material used for the inoculum was taken from an inoculated case of the disease at an early stage (Sutton's method), the attack produced in the subject was too slight, or even abortive, and it failed to give subsequent immunity. Variolation with minor technical modifications continued to be practised in England until it was gradually replaced by vaccination, as the result of Jenner's experiments, published in 1798. The advantages of vaccination are clear, but there is, nevertheless, evidence in the report quoted below, as well as in the works of Woodville and other eighteenth century writers, that the previous method of inoculation, with the virus of true small-pox, was a public health measure of some importance in its day.

Text of the Report

Stripped of the proud and generous rhetoric of the eighteenth century, the report of the "Middlesex County Hospital for Small-pox" of 180 years ago would bear a remarkable resemblance to one on the activities of a well-administered charity organization of our own time. There are passages, too, which recall to an amusing extent the sense, and even the phrasing, of some of our modern official or semi-official publications dealing with public health matters. I have modernized the spelling of a few words and condensed the very open paragraphing of the original account, but otherwise the quotations are intact.

"This excellent charity was instituted in the year 1746, supported by a subscription then made by several noblemen, gentlemen and ladies, who were desirous that a charity useful in itself, and so beneficial to the public, might be begun near this great metropolis, there not being any hospital of this kind in Europe. The relief of the necessitous under that severe, nauseous, and frequent distemper, the small-pox, is a work of charity so evidently attended with many beneficial circumstances, as well to the public as to the unhappy objects, that it is in reality not a little strange that the establishing a fund for such a charity should be a design of no longer standing. It is universally agreed that, amongst all distempers to which Providence has made the human body liable, there is none so

* Woodville, W. (1796). *History of the Inoculation of the Small-pox in Great Britain*, London.

† Creighton, C. (1894). *History of Epidemics in Britain*, Cambridge.