should require the minimum number of attendances ; in addition the cost should not be high. The combination of framycetin, gramicidin, and dexamethasone meets these requirements.

The concept of otomycosis as a commonly occurring disease has been examined. Further evidence must be awaited before conclusions can be drawn, but the weight of evidence is not at the moment in its favour.

My thanks are due to Dr. J. Fulton Christie, in whose department at Glasgow Western Infirmary the trial was carried out, and to Dr. G. C. McKinlay and Dr. W. G. Hood for providing clinical material. Mr. E. Godfrey Collins (Aberdeen) and Dr. I. Simson Hall (Edinburgh) advised upon the preparation of the paper. Roussel Laboratories provided the sofradex compound employed in this trial.

REFERENCES

- Akroyd, R. (1958). *Practitioner*, **181**, 603.
 — (1959). *J. Laryng.*, **73**, 544.
 Bihari, J. (1957). *Brit. med. J.*, **2**, 623.
Brit. med. J., 1961, **1**, 1447.
 Burrows, D. (1958). *Brit. med. J.*, **2**, 428.
 Church, R. (1954). *Ibid.*, **1**, 314.
 Collins, E. G. (1959). *Practitioner*, **183**, 699.
 Conley, J. J. (1948). *Arch. Otolaryng.* (Chicago), **47**, 721.
 Daggett, W. I. (1942). *J. Laryng.*, **57**, 427.
 Fabricant, N. D., and Perlstein, M. A. (1949). *Arch. Otolaryng.*, **49**, 201.
 Farrar, D. A. T. (1954). *Brit. med. J.*, **2**, 629.
 Gregson, A. E., and La Touche, C. J. (1961). *J. Laryng.*, **75**, 45, 167.
 Jenkins, B. H. (1961). *J. Amer. med. Ass.*, **175**, 402.
 Keogh, C., and Russell, B. (1956). *Brit. med. J.*, **1**, 1068.
 Kile, R. L., Welsh, A. L., and McAfee, G. D. (1950). *Arch. Derm. Syph.* (Chicago), **62**, 911.
 Lumsden, R. B. (1951). *J. Laryng.*, **65**, 33.
 Maccabe, A. F. (1959). *Practitioner*, **182**, 628.
 Peterkin, G. A. G. (1959). *Arch. Derm.* (Chicago), **80**, 1.
 Rattner, H. (1955). *Calif. Med.*, **83**, 331.
 Senturia, B. H., and Alford, V. (1954). *Laryngoscope* (St. Louis), **64**, 834.
 Stewart, J. P. (1951). *J. Laryng.*, **65**, 24.
 Stride, R. D. (1959). *Ibid.*, **73**, 48.
 — (1960). *Ibid.*, **74**, 531.
 Sulzberger, M. B., and Baer, R. L. (1948). *Arch. Derm. Syph.* (Chicago), **58**, 224.
 — Witten, V. H., and Smith, C. C. (1953). *J. Amer. med. Ass.*, **151**, 468.
 Syverton, J. T., Hess, W. R., and Krafchuk, J. (1946). *Arch. Otolaryng.* (Chicago), **43**, 213.
 Welsh, A. L., and Ede, M. (1955). *Ohio St. med. J.*, **51**, 350.
 Witten, V. H. (1955). *Ann. N.Y. Acad. Sci.*, **61**, 534.

"Never, I suppose, in the history of medical education has so much thought been given to the question of the content and form of medical teaching," said Professor E. G. Sayers, Dean of the Otago Medical School, in the course of his George Adlington Syme Oration at the conference of the Royal Australasian College of Surgeons in Wellington on January 30. New concepts were current about the whole philosophy of undergraduate teaching in medicine ; there was a revaluation of what sort of graduate a medical school should aim to produce and a recognition of the real problems of the medical student. Professor Sayers proceeded to define the aims of medical education which he believed would be generally acceptable. In addition to acquiring the indispensable basic skills and attitudes he said that the student should be helped to learn to regard patients not as "cases" but as persons, and to give due consideration to their personal and social background ; habits of self-education should be established so that the student would continue to educate himself after graduation and realize that he would for the rest of his life have to be a student, continually revising his knowledge and opinions ; the student should be helped to learn and practise the traditional ethical principles of his profession in reference to patients, his colleagues, and the community ; he should be encouraged to develop interests outside medicine and to build his medical knowledge on a basis of wide general reading and an acquaintance with the liberal arts and general science.

GALACTORRHOEA

BY

A. E. DORMER, M.D., M.R.C.P.
 Senior Registrar

AND

R. W. E. WATTS, M.D., Ph.D., M.R.C.P.
 Senior Lecturer
 The Medical Professorial Unit, St. Bartholomew's
 Hospital, London

Oestrogens, progesterone, adrenocortical steroids, and growth hormone are necessary for normal mammary gland development, and lactation follows the action of prolactin (luteotrophin) on the hormonally prepared breast. Milk ejection is brought about by oxytocin, which is liberated from the posterior lobe of the pituitary in response to a neurohumoral reflex initiated in the nipple. The factors which regulate the output of prolactin from the alpha (eosinophil) cells of the pituitary are obscure ; Everett (1956) concluded that this was largely independent of hypothalamic control, but recent experimental work suggests that the hypothalamic centres are involved in both milk secretion and milk ejection (McCann, Mack, and Gale, 1959 ; Linzell, 1959). Oxytocin may also cause prolactin liberation (Benson and Folley, 1956).

Galactorrhoea, or lactation which is not a physiological concomitant of pregnancy, is uncommon and may be associated with amenorrhoea as in the syndromes described by Chiari, Braun, and Spaeth (1852-5), Frommel (1882), and Forbes, Henneman, Griswold, and Albright (1954). This report describes three cases which presented some unusual features.

Case 1

A woman aged 38 was admitted to hospital in August, 1960, for the treatment of galactorrhoea. Menstruation lasting three days every 28 days began when she was aged 14 years. Her first pregnancy in 1943 resulted in a normal full-term male child which she breast-fed for nine months, and lactation persisted thereafter virtually unchanged. She was delivered of a second normal boy in 1944. This child was also breast-fed for nine months, after which lactation continued. Early in 1945 she miscarried at the tenth week of pregnancy, but later that year gave birth to a normal full-term girl whom she breast-fed for nine months. Lactation continued, and her weight which had remained basically steady at about 98 lb. (44.5 kg.) began to rise progressively. A fifth pregnancy ended in a breech still-birth in 1946. After this she was given tablets, the nature of which is unknown, for several weeks ; lactation decreased temporarily in association with this but never stopped completely. Regular menstruation was always re-established "within a few months" of delivery.

In June, 1953, when the patient was 31, menstruation ceased, although she continued to be aware of monthly abdominal discomfort. Regular sexual intercourse continued, no contraceptives were used, but pregnancy did not result. She first complained of tender lumps in the breasts and was seen by one of us in May, 1958 ; manipulation caused the discharge of milk and made the lumps disappear.

When she was admitted to hospital in 1960 the lactation was sufficient to saturate her clothes and cause social embarrassment, and milk was forcibly ejected during bathing or if the breasts were handled. On examination she was obese, weight 187 lb. (84.8 kg.) ; height 60 in. (152.5 cm.) ; the body proportions were normal—half-span 30½ in.

(77.5 cm.), crown-pubis and pubis-heel distances both 30 in. (76 cm.)—there were no cutaneous striae or other cutaneous abnormalities, and her hair was normally distributed and of normal texture. The breasts were of moderate size and milk could be expressed easily from both nipples; the appearance of the areolae resembled that usually seen during physiological lactation. There were no other abnormal physical findings; blood-pressure was 140/95 mm. Hg. Pelvic examination under anaesthesia (Mr. J. Beattie) demonstrated the presence of a fibromyoma 3 in. (7 cm.) in diameter attached to the uterus; the ovaries were not palpable.

Investigations.—Blood count normal; E.S.R. 15 mm. in one hour (Westergren); blood group A Rh+; blood Wassermann and Reiter's protein complement-fixation reaction negative; urinalysis normal; plasma protein-bound iodine 5 µg./100 ml.; serum inorganic phosphate 3.8 mg./100 ml. (as P); vaginal smear indicated low oestrin activity. The breast secretion resembled milk in appearance; it contained protein, and fat globules were demonstrated microscopically. Chest radiographs were normal, and the pituitary fossa was of normal contour but possibly slightly enlarged (maximal longitudinal diameter 15 mm., depth 12 mm.). The visual fields were normal (examination with Bjerrum screen and 2:2,000 white and 10:2,000 red test objects). The 24-hour urinary steroid excretions, measured by the Norymberski method, were: 17-ketogenic steroids 8.5 mg./24 hr., 17-hydroxycorticoids 7.3 mg./24 hr., and 17-ketosteroids 14.9 mg./24 hr. (this had been 12.1 mg./24 hr. by the M.R.C. method in 1958). An oral glucose-tolerance test with 50 mg. of glucose gave blood-sugar levels at half-hourly intervals (with a fasting level of 112 mg./100 ml.) of 112, 124, 108, and 84 mg./100 ml. respectively, and the response to insulin (4 units intravenously) was 83, 73, 83, 98, 93, and 122 mg./100 ml. respectively from a fasting level of 122 mg./100 ml. The urinary gonadotrophin excretion was low—less than 10 mouse units per 24 hours (Dr. G. I. M. Swyer).

A 1,000-calorie diet was administered during her stay in hospital (August 26 to October 25) and her weight fell to 169 lb. (76.7 kg.). She received hexoestrol dipropionate (15 mg.) intramuscularly on September 17 and 22; this did not influence the lactation appreciably, but uterine bleeding, presumably due to oestrogen withdrawal, occurred from October 12 to 15.

The pituitary gland was irradiated by Mr. I. G. Williams (2,000 r 1 MeV x rays were given through two ports) during the period September 28 to October 25, the course being interrupted for five days from October 15 because of slight swelling of the upper part of the parotid gland. Lactation from the left and right breasts stopped on October 16 and 23 respectively.

When next seen (November 25) there was no lumpiness or spontaneous discharge of milk from the breasts, although a small amount of milky fluid could be expressed from the right breast. In January, 1961, a little milk could be expressed from both breasts and on August 22, 1961, some milk could be expressed from both breasts with firm pressure, but this was not sufficient to trouble the patient. Amenorrhoea has persisted, and her clinical state has remained otherwise unaltered.

Case 2

This patient was born in 1932, and when seen in September, 1960, was complaining of persistent lactation. Her first child, who was born in 1950, had been breast-fed for two weeks; her subsequent obstetric history comprised a stillbirth in 1952 and two other normal pregnancies and confinements in 1955 and 1958, the children being breast-fed for two weeks and four days respectively. Lactation had persisted since the last delivery; it had never been sufficient to affect her clothing, nor had the breasts been tender or lumpy, but milk could always be expressed easily. Menstruation (7 days every 28 days) began when she was 16 years

old; it returned unchanged within a few months of each pregnancy, but had diminished (to 4 days in 28 days) during the year prior to being seen. There had been much unresolved anxiety concerning domestic and sexual relationships since her last pregnancy.

On examination she appeared well; there was no obesity—weight 128 lb. (58 kg.)—and her hair was normal in texture and distribution. The breasts appeared normal, but milk could be expressed easily from all quadrants. No other abnormalities were detected on physical examination, which included an examination of the pelvis by Mr. G. L. Bourne. Blood-pressure was 115/60 mm. Hg; urine was normal; the pituitary fossa was of normal size and contour (maximum longitudinal diameter 10 mm., depth 8 mm.); and the urinary excretion of 17-ketosteroids was 8.8 mg./24 hr. (M.R.C. method).

Case 3

The patient was born in 1915 and was seen on account of vague abdominal pain in 1961. Menstruation lasting three to four days every 28 days began when she was 13 years old. She had had two normal pregnancies and confinements 25 and 21 years previously and one miscarriage. Regular menstruation continued until the menopause, which had occurred in 1959, and from this time her breasts gradually increased in size. A milk discharge from both breasts was first noticed six months after the menopause and 18 months before she attended hospital. Although the breasts had not felt tender or engorged she had deliberately expressed milk on several occasions during the latter period. A fibromyoma 3 in. (7.5 cm.) in diameter had been detected eight years previously, but no treatment had proved necessary for this.

Physical examination revealed generalized obesity—weight 161 lb. (73 kg.)—the breasts were large, and small amounts of milk could be expressed. There were no other abnormalities. Blood-pressure was 130/80 mm. Hg. The pituitary fossa appeared normal on radiological examination (maximum longitudinal diameter 12 mm., depth 9 mm.), vaginal smears showed low oestrin activity, and the urinary gonadotrophin excretion was 40 mouse units per 24 hours (Dr. G. I. M. Swyer), a normal post-menopausal level.

Specific treatment was not thought to be necessary in either Case 2 or Case 3.

Discussion

Galactorrhoea has been described in association with intracranial conditions, pineal tumours (Oestreich and Slawy, 1899), benign intracranial hypertension (Pater-son, Depasquale, and Mann, 1961), and as a sequel of viral encephalitis (Riese, 1928). Other cases have been associated with acromegaly (Carnot and Bouttier, 1930; Davidoff, 1940), testicular chorionepithelioma (Cooke, 1915), and adrenal tumour (Weber, 1926). Wilkins (1957) and Van Wyk and Grumbach (1960) describe a syndrome of galactorrhoea, hypothyroidism, and precocious puberty in girls, all the manifestations of which were relieved by thyroxine administration. Another group of patients in whom galactorrhoea, hyperthyroidism, and abnormal uterine haemorrhage were associated was reported by Zondek, Bromberg, and Rozin (1951). Reserpine and the phenothiazine group of drugs may also cause galactorrhoea (Platt and Sears, 1956; Johnson, Poshychinda, McCormick, and Hamblen, 1960), and other cases have been attributed to prolonged stimulation of the nipple (Knott, 1907; Phillips, 1960) or to surgical interference with the thoracic wall (Grossman, Buchberg, Brecher, and Hallinger, 1950). The condition is also occasionally encountered in the neonatal period.

The syndrome of galactorrhoea and amenorrhoea, with uterine and ovarian atrophy following childbirth

but unassociated with prolonged nursing, is usually referred to as the Chiari-Frommel syndrome (Chiari *et al.*, 1852-5; Frommel, 1882; Sharpe, 1935). These cases are usually distinguished from the so-called Forbes-Albright syndrome (Forbes *et al.*, 1954) in which similar manifestations do not follow childbirth (see, for example, Jeffcoate, 1958). It is, however, not certain that these two groups of cases should be classified separately. Forbes *et al.* (1954) described 15 cases; nine of these patients were nulliparae, and in six the symptoms followed pregnancy. All these patients excreted low levels of gonadotrophin (in contrast to normally lactating women with amenorrhoea), many were overweight, while some were hirsute and had slightly raised 17-ketosteroid excretions. Six of the nulliparae and two of the parous patients had evidence of a pituitary tumour, which was known to be a chromophobe adenoma in three of them.

Potter (1944) and Mendel (1946) record cases in which menstruation was resumed and lactation ceased spontaneously after four and two years respectively; Potter's patient also became pregnant. Toaff and Sadovsky (1951) described the case of a patient with pituitary basophil adenoma who developed galactorrhoea and amenorrhoea five years post partum and in whom menstruation was resumed after removal of the tumour. Greenblatt, Carmona, and Hagler's (1956) cases had suggestive evidence of a pituitary tumour, low levels of plasma protein-bound iodine, low excretions of gonadotrophin, oestrogen, and pregnanediol with normal adrenocortical function, and raised levels of prolactin excretion.

Breast-feeding was not continued for an abnormally long time by any of our patients, and although they all admitted expressing milk manually from time to time this was clearly a sequel and not an antecedent of the galactorrhoea. The vigorous expulsion of milk which occurred in Case 1 in response to minimal breast stimulation raises the possibility that there may have been excessive secretion of oxytocin as well as of prolactin in this patient. None of our patients had evidence of a pituitary tumour or of any associated gross endocrinopathy; and the obesity in Cases 1 and 3 did not resemble that seen in pituitary dysfunction. The occurrence of galactorrhoea with normal menstruation and intercurrent pregnancies (Case 1) is infrequent (Dowling, Richards, Freinkel, and Ingbar, 1961). However, menstruation stopped unusually early, the ovaries were atrophic, and the gonadotrophin excretion was abnormally low, as in the cases described by Forbes *et al.* (1954), by the time she came under our care.

It is of interest that the amount of milk secreted was not greatly influenced by the pregnancies, and this suggests that it may have been mediated by autonomous pituitary activity. Our Case 2, who also had galactorrhoea, which began after a normal pregnancy and confinement, may represent an earlier stage in the evolution of the condition affecting Case 1. It may be significant in this connexion that menstruation was diminished in Case 2 during the past year, having been re-established unchanged after her last pregnancy. Case 3 presents the unique feature that galactorrhoea began six months after a normal menopause as judged clinically and on the basis of her gonadotrophin excretion.

Pituitary irradiation proved to be a useful line of treatment in Case 1, and we think that it is justified in the rare cases where the galactorrhoea causes gross

social embarrassment. Levin, Daughaday, and Levy (1959) found that in two patients with pituitary tumours, although the galactorrhoea could be suppressed by pituitary irradiation, menstruation was not re-established; but McCullagh, Alivisatos, and Schaffenburg (1956) report the case of a male patient whose galactorrhoea was not influenced by this treatment.

It seems that the natural history of these cases may be more protean than has previously been supposed, but their detailed endocrinological investigation is difficult in the absence of satisfactory methods of measuring prolactin and oxytocin and other possibly mammothrophic substances—for example, growth hormone—in body fluids.

Summary

Three unusual cases of galactorrhoea are described and compared with other previously recorded cases. It is emphasized that the amenorrhoea which has classically been described in association with galactorrhoea may not begin until abnormal lactation has continued for many years.

In one case pituitary irradiation almost completely abolished the galactorrhoea, but menstruation was not re-established.

We are pleased to acknowledge our indebtedness to Professor E. F. Scowen for his interest and permission to include Case 1, admitted under his care; to Mr. G. L. Bourne, who referred Case 2 to us; to Dr. A. G. Spencer, who first saw Case 3; and to Dr. G. I. M. Swyer, who performed the gonadotrophin assays.

REFERENCES

- Benson, G. K., and Folley, S. J. (1956). *Nature (Lond.)*, **177**, 700.
 Carnot, P., and Bouttier (1930). *Bull. Soc. méd. Hôp. Paris*, **54**, 392.
 Chiari, J., Braun, C., and Spaeth, J. (1852-5). *Klinik der Geburtshilfe und Gynaekologie*, p. 371. Enke, Erlangen.
 Cooke, J. V. (1915). *Bull. Johns Hopk. Hosp.*, **26**, 215.
 Davidoff, L. M. (1940). *Bull. N.Y. Acad. Med.*, **16**, 227.
 Dowling, J. T., Richards, J. B., Freinkel, N., and Ingbar, S. H. (1961). *Arch. intern. Med.*, **107**, 885.
 Everett, J. W. (1956). *Endocrinology*, **58**, 786.
 Forbes, A. P., Henneman, P. H., Griswold, G. C., and Albright, F. (1954). *J. clin. Endocr.*, **14**, 265.
 Frommel, R. (1882). *Z. Geburtsh. Gynäk.*, **7**, 305.
 Greenblatt, R. B., Carmona, N., and Hagler, W. S. (1956). *Obstet. and Gynec.*, **7**, 165.
 Grossman, S., Buchberg, A. S., Brecher, E., and Hallinger, L. M. (1950). *J. clin. Endocr.*, **10**, 729.
 Jeffcoate, T. N. A. (1958). "Disorders of Menstruation," in *British Obstetric and Gynaecological Practice*, edited by E. Holland and A. Bourne. Heinemann, London.
 Johnson, H. W., Poshyachinda, D., McCormick, G., and Hamblen, E. C. (1960). *Amer. J. Obstet. Gynec.*, **80**, 124.
 Knott, J. (1907). *Amer. Med. (Philad.)*, **13**, 373.
 Levin, M. E., Daughaday, W. H., and Levy, I. (1959). *Amer. J. Med.*, **27**, 172.
 Linzell, J. L. (1959). *Physiol. Rev.*, **39**, 534.
 McCann, S. M., Mack, R., and Gale, C. (1959). *Endocrinology*, **64**, 870.
 McCullagh, E. P., Alivisatos, J. G., and Schaffenburg, C. A. (1956). *J. clin. Endocr.*, **16**, 397.
 Mendel, E. B. (1946). *Amer. J. Obstet. Gynec.*, **51**, 889.
 Oestreich, R., and Slawyk (1899). *Virchows Arch. path. Anat.*, **157**, 475.
 Paterson, R., Depasquale, N., and Mann, S. (1961). *Medicine (Baltimore)*, **40**, 85.
 Phillips, A. F. (1960). *Brit. med. J.*, **2**, 234.
 Platt, R., and Sears, H. T. N. (1956). *Lancet*, **1**, 401.
 Potter, J. C. (1944). *Amer. J. Obstet. Gynec.*, **47**, 276.
 Riese, W. (1928). *Klin. Wschr.*, **7**, 1954.
 Sharpe, E. A. (1935). *Amer. J. Obstet. Gynec.*, **30**, 411.
 Toaff, R., and Sadovsky, A. (1951). *Harefuah*, **41**, 191.
 Van Wyk, J. J., and Grumbach, M. M. (1960). *J. Pediat.*, **57**, 416.
 Weber, F. P. (1926). *Brit. J. Derm. Syph.*, **38**, 1.
 Wilkins, L. (1957). *The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence*, 2nd ed., p. 203. Blackwell, Oxford.
 Zondek, B., Bromberg, Y. M., and Rozin, S. (1951). *J. Obstet. Gynaec. Brit. Emp.*, **58**, 525.