was our practice to give the infant the same kind of food as he had had before admission unless there was some definite contraindication. Vitamins A, B, C, and D were added to the feeds from the first day, and continued throughout the stay in hospital.

3. The early correction of fluid loss. Fluids and proteins were administered intravenously in the form of half-strength serum or plasma (diluted with Hartmann's solution) as soon as there was clinical evidence of dehydration, and in quantities sufficient to restore fluid loss and maintain the infant's daily requirements. The usual allowance of $2\frac{1}{2}$ oz. per lb. per day was made, plus an allowance of 3 to 6% of body weight for dehydration in the first 24 to 48 hours. The intravenous drip was begun with half a bottle of Hartmann's + $2\frac{1}{2}$ to 5% glucose, and serum or plasma then added (diluted to half-strength with Hartmann's). The drip was continued, giving alternate bottles of Hartmann's solution and half-strength serum or plasma, until dehydration was completely corrected and the infant was able to take and retain a dilute feed; this was generally in 1 to 3 days. Feeding was usually begun 12 to 24 hours after the commencement of intravenous therapy, and the quantity and strength of the milk feed gradually increased, the rate of the intravenous drip being adjusted accordingly.

4. Energetic measures to combat shock in those infants admitted in a state of collapse. Warmth, stimulants such as brandy and coramine, and oxygen were given, and the intravenous drip was begun immediately. Treatment in these cases was considered as urgent as in "surgical shock."

5. The combating of anaemia by routine administration of iron (in the form of a ferrous sulphate mixture) and blood transfusions as required.

6. The prevention of cross-infection; all infants were nursed in cell or barrier wards with strict bed-isolation technique, including the wearing of gowns and masks by all attendants.

Summary and Conclusions

One hundred and forty cases of diarrhoea and vomiting in infants under 15 months of age are analysed.

The cases were of average severity as judged by incidence and degree of dehydration; 69 (49.3%) were dehydrated, the maximum incidence of severity occurring in the age group 0-9 months.

There were 8 deaths, giving a case fatality of 5.7% for all cases, or 11.6% of dehydrated cases; 6 of the 8 deaths followed relapses.

There were 27 relapses. The relapse rate in the open "barrier" ward was four times that in the cell wards.

Evidence of parenteral infection was found in 124 cases, or 88.6%. The type of parenteral infection and incidence of infecting organisms are shown.

The changes in body chemistry in dehydration occurring in diarrhoea and vomiting are discussed, and the need for further research in this field is stressed.

The gratifying results obtained in this series may be attributed to: (1) the fact that the parenteral infections present were fairly easy to recognize and treat; and (2) the attention paid to the prevention or early correction of dehydration, and early return to full feeds and maintenance of nutrition. So long as the aetiology of this killing disease remains obscure, treatment of established diarrhoea and vomiting must be directed along these lines. Breast-feeding for at least the first 6 months of life remains our best-known prophylactic measure, combined with protection of the infant from exposure to infection.

We wish to express our thanks to the medical superintendent, Dr. W. Gunn, for facilities to carry out this investigation, and to the nursing staff for their unflinching co-operation. Our thanks are also due to the staff of the North-Western Group laboratory, by whom all the numerous bacteriological and biochemical investigations were performed.

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R. D. Reid and L. H. Bronstein (*J. Amer. med. Ass.*, 1944, **124**, 703), who record an illustrative case in a boy aged 2 years, state that meningococcal conjunctivitis should be suspected in cases with Gram-negative intracellular diplococci in smears of pus from the eyes when there is no obvious source of the infection. The authors' patient recovered under sulphathiazole by mouth.

INHIBITION OF LACTATION BY HEXOESTROL DIPROPIONATE

BY

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Physiology of Lactation

In the physiology of lactation both hormonal and neurogenic factors are concerned. The development of the lobule-alveolar system of the glands of the breasts during pregnancy is influenced by the ovarian hormones, oestrogen and progesterone (Nelson, 1936). After delivery the initiation and maintenance of lactation depend upon the presence of the anterior lobe of the pituitary, since hypophysectomy late in pregnancy or after parturition inhibits post-partum milk secretion (Selye, 1934). A further factor in the maintenance of established lactation is a neurogenic one—namely, the act of suckling, which reflexly stimulates the release of a lactogenic principle from the anterior pituitary. The release of the latter principle occurs only after the inhibiting effect of oestrogen is withdrawn—that is, after delivery. Oestrogens in large doses are known to inhibit lactation (Folley, 1936; Folley and Kon, 1936); this they do probably by depressing the activity of the anterior pituitary. The absence of the suckling stimulus together with the administration of an oestrogen may therefore be expected to produce inhibition of lactation.

Methods used for Inhibiting Lactation

In the past the most common method used to prevent or suppress lactation was the application of a tight breast-binder, restriction of fluids, purgation, and removal of the infant from the breast. Many cases treated in this way had painful engorgement or tenderness of the breasts; moreover, neither the severe restriction of fluids nor purgation is wise in the early puerperium. Following the observation that large doses of oestrogens suppressed lactation in the experimental animal, natural oestrogenic hormones such as oestradiol were employed to inhibit lactation clinically, and after the introduction of the synthetic oestrogens these were almost exclusively used on account of their cheapness. The one most widely employed has been stilboestrol. There are many published papers on the use of this compound in the inhibition of lactation (Abarbanel and Goodfriend, 1940; Abarbanel and Klein, 1941; Barnes, 1942; Bloom, 1941; Connally *et al.*, 1940; Davis and Boynton, 1941; Mendel, Goldman, and Caire, 1941; Mucklé, 1940; Palmer, Martin, and Fulton, 1942; Stewart and Pratt, 1941). The general opinion is that for this purpose stilboestrol is just as effective by mouth as by injection. A study of these papers reveals that: (a) stilboestrol is less effective in women already lactating; (b) a course of treatment lasts usually four to five days, and sometimes for as long as six, seven, or even ten days, the dosage ranging from 5 mg. daily to 15 mg. t.i.d.; (c) initial success is often achieved in the first few days, but the breasts may fill up four to nine days later and further treatment is then necessary (Mucklé, 1940; Palmer, Martin, and Fulton, 1942). According to Connally *et al.* (1940) stilboestrol does not completely inhibit lactation, but delays its onset to the fifth or sixth day after delivery.

Hexoestrol has also been used for the inhibition of lactation (Bishop, *et al.*, 1940; Barnes, 1942). It is given orally in a similar dosage to stilboestrol, and seems to produce much the same result. Barnes (1942) states that, weight for weight, hexoestrol is less potent than stilboestrol for the inhibition of lactation: she, however, administered both substances orally. Campbell *et al.* (1939) claim that by injection hexoestrol is more potent than stilboestrol.

Other endocrines that have been used to inhibit lactation are dienoestrol (Barnes, 1942); trichlorethylene (Macpherson and Robertson, 1939; Haultain, 1942); testosterone propionate (Kurzrok and O'Connell, 1938; Siegler and Silverstein, 1940;

Duffy and Corsaro, 1941); methyl testosterone (Kushner, 1942; Lass, 1942); and octofollin (Murphy, 1943).

Use of Hexoestrol Dipropionate

It is well known that esterification of the oestrogens retards their rate of absorption and elimination and thus prolongs their action in the body (Miescher, Scholz, and Tschopp, 1938). Dr. G. Brownlee of the Wellcome Physiological Research Laboratories converted hexoestrol into the dipropionate and submitted it to pharmacological tests. He reported that by injection hexoestrol dipropionate was one and a half to three times more potent than hexoestrol when tested on ovariectomized immature rats. By mouth hexoestrol dipropionate was not as potent as hexoestrol weight for weight, but the duration of action was twice as long. As this report was encouraging, it was decided to try the effect of hexoestrol dipropionate clinically for the suppression of lactation. It was given to separate groups of women orally in tablet form and intramuscularly in oil; but it soon became apparent that orally it was not so effective as parenterally, and the oral route was abandoned. This confirmed Dr. Brownlee's pharmacological tests.

The patients treated were those in whom it was necessary to inhibit lactation because of stillbirth, abortion, neonatal death, or cracked nipples. No other treatment was given—i.e., the breasts were not bound up, no purgatives were used, and fluids were not restricted. Results, if any, were therefore due to treatment.

Effect of Hexoestrol Dipropionate given Orally

Twenty-three patients were given hexoestrol dipropionate orally in doses varying from 10 to 20 mg., three times daily. Treatment was started in 13 cases on the first day post partum, and in 10 on the second or third day. A successful result was taken to be one in which lactation was inhibited without breast engorgement or painful breasts on or before the third day of treatment. The results are analysed in Table I.

TABLE I.—Analysis of Results of Oral Administration of Hexoestrol Dipropionate

Total No. of Cases	Successful Result on 1st Day	Successful Result on 2nd Day	Successful Result on 3rd Day	Successful Result after More than 3 Days	Failures
23	2 9%	3 13%	4 17%	10 44%	4 17%
	39%				

Using the criteria given above, it will be seen that only 9 out of 23 cases, or approximately 40%, were successful. The average total dosage in the successful cases was 90 mg., with a range of 28 to 180 mg. A successful result on the first day was obtained in 2 cases. In 10 of the series (44%) it took more than three days to inhibit lactation, and in 4 cases (17%) treatment failed to inhibit lactation. No untoward results, such as nausea or vomiting, were observed. Five of the patients had full or engorged breasts in spite of treatment.

Effect of Hexoestrol Dipropionate given Parenterally

Forty-four cases were treated with hexoestrol dipropionate in oil by intramuscular injection. Repeated injections were tried at first, but it was eventually found that in most cases a single injection of 12.5 mg. was sufficient to inhibit lactation if given within three days of delivery. The results are summarized in Table II.

TABLE II.—Analysis of Results of Intramuscular Administration of Hexoestrol Dipropionate

Total No. of Cases	Success after 1 Day's Treatment (1 Injection)	Success after 2 Days' Treatment (2 Injections)	Success after 3 Days' Treatment (3 Injections)	Success after More than 3 Days' Treatment	Cases in which Treatment was Repeated	Failures
44	29 (66%)	2 (5%)	4 (9%)	8 (18%)	3 (7%)	1 (2%)

The day of the puerperium on which treatment was started did not seem to affect the results appreciably, as Table III shows.

TABLE III

Day of Puerperium Treatment Started	No. of Cases	Success after 1 Day's Treatment (1 Injection)	Success after 2 Days' Treatment (2 Injections)	Success after 3 Days' Treatment (3 Injections)	Success after More than 3 Days' Treatment	Cases given Second Course of Treatment	Failures
1st	12	8	—	—	4	—	—
2nd	17	11	—	2	3	—	1
3rd	8	7	1	—	—	—	—
4th	2	1	—	—	—	—	—
5th	2	1	—	—	1	—	—
18th	1	—	—	—	—	—	—
19th	1	—	—	—	—	—	—
21st	1	1	—	—	—	—	—
Totals	44	29	2	4	8	3	1
Percentage		66%	5%	9%	18%	7%	2%
		80%					

In five cases hexoestrol dipropionate was given after lactation had been established—namely, on the 5th, 18th, 19th, and 21st days post partum. In four cases lactation was suppressed on or before the third day, and in one case on the fifth day. Four cases required only one injection, and one case required two injections.

A small series of patients received 10 to 15 mg. of hexoestrol in oil as a control, but the results were no better than those obtained with stilboestrol or other oestrogens by mouth. Daily injections over a period of many days were necessary to inhibit lactation.

Conclusions

These results show that a single injection of hexoestrol dipropionate in oil inhibited lactation in 66% of the cases. The dose used was generally 12.5 mg. If a successful result is taken to be inhibition of lactation without breast engorgement on or before the third day after starting treatment, then 35 cases out of 44 (80%) were successful. Eight cases (18%) required treatment for more than three days, and there was one failure—a case in which the breasts were engorged and there was a slight flow of milk a fortnight after beginning treatment. A second course of treatment was needed in 3 cases only (7%). In no other cases were the breasts tender or engorged. With the suppression or inhibition of lactation the breasts became soft and comfortable. No unpleasant side-effects were observed in any of the patients. The results were vastly superior to those obtained with hexoestrol dipropionate by mouth. Administered by the latter route, a course given over several days was invariably necessary. In only 2 out of 23 cases (9%) was a one-day oral course effective in inhibiting lactation, and in only 9 cases (39%) was a three-days course effective.

Discussion

For the suppression of lactation hexoestrol dipropionate given by injection is superior to stilboestrol or hexoestrol by mouth or by injection. With stilboestrol and hexoestrol a course of several days' treatment is necessary, and a repeat course is often needed several days later owing to secondary filling. Thus Mucklé (1940) found that 40% of his 200 cases given a course of stilboestrol by mouth required a second course; Connally *et al.* (1940) found suppression of lactation with stilboestrol incomplete; and Barnes (1942) states that a quarter of her cases receiving stilboestrol required a repeated course of treatment. Stilboestrol is also not effective in women already lactating (Stewart and Pratt, 1941). In five of the cases recorded in the present paper one or two injections of hexoestrol dipropionate suppressed established lactation in a few days. According to Barnes (1942), dienoestrol and hexoestrol are not as effective as stilboestrol in inhibiting lactation.

Testosterone and methyl testosterone are stated to be more effective than stilboestrol. Duffy and Corsaro (1941) claim that 50 to 75 mg. of testosterone, in 25-mg. doses, inhibits lactation in 24 to 48 hours if given within the third or fourth day of delivery, but is ineffective on the first day or when lactation is established. The same authors gave methyl testosterone orally in 25-mg. doses four-hourly for two days with similar results. Kurzrok and O'Connell (1938), however, found that 70% of their cases required two daily injections of 10 to 25 mg. of testosterone dipropionate for periods of from three to seven

days. This period was decreased if doses of 25 to 50 mg. were given (Birnberg, Kurzrok, and Klor, 1940). Siegler and Silverstein (1940) inhibited lactation by giving total doses of 25 to 125 mg. of testosterone dipropionate in divided doses every 12 hours, with a total of three to five injections. Lass (1942) states that methyl testosterone in repeated doses of 25 mg. inhibits lactation in 48 hours; total dosage was from 250 to 350 mg. In 7 out of 25 cases methyl testosterone was effective on the first day.

A new synthetic oestrogen—octofollin or 2:4-di-(*p*-hydroxyphenyl)-3-ethyl hexane—has recently been used for the inhibition of lactation (Murphy, 1943). This, given over a period of four days in doses of 5 m.g. t.i.d., yields results similar to those obtained with stilboestrol.

From this discussion it is clear that hexoestrol dipropionate given parenterally is more effective for the inhibition of lactation than the other synthetic oestrogens and testosterone or its derivatives. With the possible exception of methyl testosterone none of these is effective in inhibiting lactation on the first day of treatment. The use of synthetic androgens in high dosage is ruled out on the grounds of expense.

Summary

A single intramuscular injection of 12.5 mg. of hexoestrol dipropionate inhibited lactation in 66% of a series of 44 mothers shortly after childbirth. When given within the first three days of delivery lactation did not occur, and there were no signs of breast engorgement or discomfort. Of the remaining 34% all but 2% ultimately responded to repeated injections. Only 18% required treatment for more than three days.

A further course of injections, given to suppress "secondary filling," was necessary in only 7% of the cases. This compares well with the figure of 25 to 45% for stilboestrol.

Hexoestrol dipropionate, given intramuscularly in one or two doses, was effective in suppressing lactation in five cases in which it had already been established.

Hexoestrol dipropionate given by mouth is not so satisfactory as when given by injection.

Literature on the inhibition of lactation by oestrogens and androgens is reviewed.

Thanks are due to the members of the resident medical staff of the Mothers' Hospital, Clapton, for their assistance and care in keeping records of the cases.

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The 208th session of the Royal Medical Society of Edinburgh will open on Friday, Oct. 13, with an inaugural address by Lord Moran, P.R.C.P., on "The Anatomy of Courage." Other addresses will be given on Oct. 27, by Sir Joseph Barcroft, on "Problems in Foetal Life"; on Nov. 10, by Sir Alexander Fleming, on "Penicillin"; on Nov. 24, by Prof. J. H. Gaddum, on "The Discovery of New Remedies"; on Jan. 12, by Sir John Boyd Orr, on "The Future of Medicine"; on Jan. 26, by Lieut.-Gen. Sir Alexander Hood, on "The Army Medical Services in Peace and War"; on Feb. 2, by the Right Hon. Walter Elliot, on "Medicine and the State"; and on Feb. 16, by Col. J. C. Kimbrough, U.S. Army Medical Corps, on "Wounds of the Genito-urinary Tract in Modern Warfare."

FACTORS INFLUENCING DERMATITIS IN COAL-MINERS

BY

R. B. KNOWLES, M.D.

Many of the dermatoses to which miners are subject may occur in any person, whatever his trade, but some are directly or indirectly associated with the conditions under which these men work. The latter forms may be divided into two main groups: (I) those due, in the main, to trauma and infection, which might be called "the stigmata of miners"; (II) cases of dermatitis in the usually accepted sense, including occupational dermatitis.

Group I

The blue-black scar present on the skins of most miners is due to the fine particles of coal-dust which enter a wound at the time of injury. Callosities on the hands are common, and are to be seen across the heads of the metacarpals and on the inner side of the thumb, where the tools set up constant friction. The boots cause thickenings of the skin on the front and back of the ankle.

Bursae, true and false, play a part in the infections and injuries to which coal-miners are liable. False bursae may occur along the heads of the metacarpals, producing, when infected, the "beat-hand" of the miner. Bursae at the patella and olecranon may become the "beat-knee" and the "beat-elbow." Foreign bodies between the knee-pads and the skin sometimes help in the production of "beat-knee."

These infections are not likely to occur without some abrasion of the skin, which allows the entry of bacteria and provides a medium suitable for their growth. Various kinds of pyoderma may thus be produced either by staphylococci (boils, pustules, folliculitis, subcutaneous abscesses, and ulcers) or by streptococci (vesicles, bullae, impetigo, ecthyma, with lymphangitis and cellulitis, onychia, and whitlow). "Infected abrasions" are a very common condition among miners. Acid burns on the buttock, caused by the leakage of sulphuric acid from the lamp-battery, are also seen.

Group II

Clinically, acute cases are often eczematous, and chronic cases, as a result of constant irritation and scratching, may become lichenified. Starting with erythema, the dermatitis may become vesicular, weeping, scaly, papular, pustular, and follicular. Occasionally there is fissuring of the palm. The chief symptoms are itching, soreness, and pain.

Most of these cases of dermatitis involve chiefly the hands and forearms, the feet and legs; but some begin on the trunk and others attack the trunk after starting elsewhere. Sometimes an intertrigo occurs in the axillae or groins, or between the toes. Encouraged by moisture, heat, and friction, streptococci produce this intertrigo of the skin; or it may be due to a monilial infection and occur in the gluteal folds. In coal-miners, intertrigo may also be found on the outside of the forearm and the inner part of the thigh, as the result of constant friction of the arm against the thigh when using pick and shovel.

An eczematous eruption in the external auditory meatus may be caused by particles of stone and coal falling into the ear which is uppermost when a collier is in the reclining position.

There are few miners who do not wear a belt, and friction between this and the skin may determine the onset of a dermatitis around the lower abdomen. Fungous infection of the feet has recently become prevalent, and its spread appears to be facilitated by pit-head baths. It is more common in the summer months, and occurs in three principal types: (a) Sudden white skin between and underneath the toes, especially in the fourth interdigital cleft. The infection may spread and produce pustules on the soles of the feet. (b) Superficial scaling of parts of the hands or feet. (c) An eruption of deeply set vesicles on the soles of the feet: this is the most common type. The infection may also spread to the groins, to produce tinea cruris; the axillae, perineum, natal cleft, and thighs may be involved.

Improper treatment of wounds or skin lesions—e.g., by sulphur ointment, iodine, or antiseptics—may produce dermatitis.