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INFANTILE DIARRHOEA AND VOMITING

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This series comprises 140 cases of infantile diarrhoea and vomiting treated at the North-Western Hospital between June, 1943, and February, 1944, inclusive.

Summary of Cases

Age.—The infants were all under 15 months of age. Older children were excluded, since the disease is less common and invariably milder after the age of 15 months. When divided into five age groups, of 3 months each, 115—i.e., 82.1%—of the infants were in the first three age groups (0 to 9 months), the incidence falling sharply after 9 months. The severity, as judged by dehydration, was also greatest in the first 9 months of life, with 56.5% of dehydrated infants as compared with 16% in the age groups IV–V (9 to 15 months). This incidence corresponds with that found by Campbell and Cunningham (1941). There were no deaths among the infants over 6 months of age (Tables I and II).

TABLE I.—*Distribution in Age Groups: Death and Dehydration Rate in Each Age Group*

Age Groups	No. of Cases	Deaths		Dehydration		% Deaths among Dehydrated
		No.	Case Fatality %	No.	%	
I—0–3 months ..	38	4	10.5	23	60.5	17.3
II—3–6 ..	49	4	8.1	27	55.1	14.8
III—6–9 ..	28	0	0	15	53.5	0
IV—9–12 ..	13	0	0	3	23.6	0
V—12–15 ..	12	0	0	1	8.3	0
Total ..	140	8	5.7	69	49.3	11.6

TABLE II.—*Incidence, Dehydration, and Mortality in Infants Under and Over 9 Months*

Age in Months	No. of Cases	Dehydration		Deaths	Case Fatality %	% Deaths among Dehydrated
		No.	%			
0–9	115	65	56.5	8	6.9	12.3
9–15	25	4	16	0	0	0
Total	140	69	49.3	8	5.7	11.6

Prematurity.—There were 8 premature infants in this series, all under 7 weeks old on admission. All 8 were dehydrated, and 7 required intravenous therapy. There were 3 deaths. The illness in all these cases was very severe, and convalescence slow. It is of interest to note that 3 of these babies had severe anaemia requiring blood transfusions, and that slow-drip transfusions of 200 to 250 c.cm. of blood were well tolerated after initial correction of fluid loss.

Sex.—Males predominated in the ratio of 3:2.

Season.—No deductions can be drawn from the number of admissions per month, as these were governed by external factors. Severity, as judged by dehydration, appeared to be highest in the winter months; but, again, no deductions can be made, as this series does not include the spring quarter.

Environment.—Twenty infants were admitted from institutions; of these, 14 were dehydrated, 8 required intravenous therapy, and

1 died. Seventeen were admitted from other hospitals, of whom 12 were dehydrated and required intravenous therapy, and 1 died. The remaining 103 infants were admitted from home; of these, 43 were dehydrated and 6 died. We are unable to say what proportion of this last group were attending day nurseries.

Breast-feeding.—In this series 17 babies were breast-fed—8 wholly and 9 partially. This rather high incidence (12.1%) may be partly accounted for by the fact that cases were admitted from a maternity unit. Ages ranged from 1 week to 5 months in the case of the fully breast-fed infants, and from 3 to 10 months in the partially breast-fed babies. One fully and 4 partially breast-fed infants were dehydrated and required intravenous therapy. Breast-feeding was continued wherever possible. There were no deaths in this group. The illness was seldom so severe as in the artificially fed babies, and recovery was quicker and usually uncomplicated.

Dehydration and Severity.—Forty-nine infants were dehydrated on or soon after admission, and a further 20 became dehydrated more than forty-eight hours after admission—i.e., 69 cases in all, or 49.3% of the total. Of these, 26 showed evidence of extreme fluid loss, and 11 of them were collapsed on admission, exhibiting unmistakable signs of shock—cold, clammy skin; subnormal temperature; thin, thready, or imperceptible pulse; cyanosis of lips and extremities; shallow or sighing respiration—in addition to the usually severe dehydration. None of these 11 died. In 6 cases “orange” stools—an unfavourable prognostic sign—appeared for more than twenty-four hours during the course of the illness; 5 of these patients recovered and 1 died.

Duration.—The average stay in hospital was 30.2 days. No deductions can be drawn from this figure as many infants were, for administrative reasons, kept in hospital after recovery.

Mortality and Cause of Death.—There were 8 deaths in this series, giving a case fatality of 5.7% for all cases, or 11.6% of dehydrated cases. All these 8 infants were under 6 months of age, and 6 of the 8 deaths followed relapses. Post-mortem examinations were performed in 7 cases, and the causes of death found were: suppurative pericarditis (*Staph. aureus*), 1; circulatory failure due to excessive parenteral fluids, 2. The remainder of the deaths were classified as due to gastro-enteritis, complicated by otitis media in 1 case and by whooping-cough and secondary pneumonia in another.

Parenteral Infection

An attempt was made to investigate the presence and type of parenteral infection in these cases, based on the following criteria: (1) A history of parenteral infection preceding or concurrent with the onset of diarrhoea and vomiting. (2) Clinical signs of parenteral infection on admission—i.e., rhinitis, tonsillitis, otitis media, bronchitis, furunculosis, etc. (3) Bacteriological confirmation: nose, throat, and post-nasal swabs, and faeces and rectal swabs were taken from all infants on admission, and at intervals throughout the course of the illness, for bacteriological examination. In addition, swabs were taken from any discharge—e.g., pustules, otorrhoea. The urine was investigated in a few cases only, owing to the difficulty in collecting sterile samples of urine from babies with diarrhoea. All infants showing bacteriological evidence of intestinal infections such as bacillary dysentery and giardiasis were excluded from this series.

1. In 36 cases there was a history of parenteral infection immediately before the onset of diarrhoea and vomiting, and in 58 cases accompanying this—a total of 94 cases, or 67.1% of all. In many instances upper respiratory infections had been present in other members of the family before the infant's illness.

2. In 124 cases (88.6%) there was definite clinical evidence of parenteral infection on admission, mainly of the respiratory tract. There were 60 cases of otitis media. Only those cases in which a purulent otorrhoea occurred spontaneously or was found at myringotomy were included under the heading of otitis media. In 49 of these otorrhoea was present on, or within forty-eight hours of, admission. In the remaining 11 cases the otorrhoea appeared in 5 to 20 days; in all these 11 there had been evidence of upper respiratory infection on admission. Myringotomy was performed in 38 cases, and bilateral mastoidectomy in 11. Table III shows

TABLE III.—Incidence and Type of Parenteral Infection present in 140 Cases

Parenteral Infection	No.
Upper respiratory infection	29
Tonsillitis	12
Otitis media	20
Otitis media + other infections	40
Bronchitis	11
Pneumonia	2
Skin infections	8
Stomatitis	1
Conjunctivitis	1
Total	124

Note: Upper respiratory infection = rhinitis and pharyngitis.

the type and incidence of parenteral infection present in the whole series. In 88 cases (62.8%) pyrexia (temperature above 99° F.) occurred within twenty-four hours of admission. In 80 of these the pyrexia was associated with other evidence of parenteral infection, and in 8 no signs of parenteral infection could be found. Subnormal temperatures were observed in the 11 infants admitted in a state of shock. Temperatures of 101° to 103° F. sometimes appeared after the parenteral administration of plasma; we have tried to separate these from the initial pyrexia, which seemed to be due to the parenteral infection. It is noteworthy that 19 of 27 relapses (70.4%) were preceded by signs of parenteral infection and a rise of temperature above 99° F. Very often there was only a slight pyrexia of less than twenty-four hours' duration, which was followed in 24 to 72 hours by a relapse of the diarrhoea and vomiting, in some cases surprisingly severe, and with no further rise of temperature until the final agonal peak in the cases ending fatally.

3. Table IV shows the incidence and type of pathogenic organisms cultured from the upper respiratory tract on admission. The presence of *Staph. aureus* in the nose only was not regarded as significant, and these results are omitted from this table. The mere presence of

TABLE IV.—Incidence and Type of Pathogenic Organisms Cultured from the Upper Respiratory Tract

Organism	N	T	P.N.	P.N. + {N or T}	Ears	Ears + {N or T or P.N.	Skins	Total
Haem. strep...	2	6	4	11	0	2	0	25
Pneumo...	2	1	4	5	7	3	0	22
Staph. aureus		3	3	7	8	13	2	33
Total	4	10	11	23	15	15	2	80

Note: N = Nose. T = Throat. P.N. = Post-nasal.

these organisms in the nasopharynx does not necessarily imply an infection with them, but we feel that they are of significance if taken in conjunction with the clinical findings.

The discrepancy between the positive bacteriological findings in the ear discharges—30—and the actual number of otorrhoeas—60—may be partly explained by the difficulty of obtaining sterile cotton-wool swabs small enough to be passed through the infant's narrow meatus to reach the perforation or myringotomy wound. In the remaining cases only saprophytic organisms such as *Staph. albus*, diphtheroids, etc., were recovered on culture. Among the 11 mastoidectomies, swabs from the bone at operation were sterile in 7 cases. In the remaining 4, pneumococci, haemolytic streptococci, *Staph. aureus*, and *B. coli* were found each in one case. But although the incidence of bacteriologically proved mastoiditis may be no higher in diarrhoea and vomiting than that following otitis media in older children, mastoidectomy should always be considered in those cases of diarrhoea and vomiting in which pyrexia persists and the child fails to respond to sulphonamide and intravenous plasma therapy, provided the ear has shown some signs of inflammation and no other focus of infection has been demonstrated. The

operation carries very little risk in experienced hands after careful pre-operative correction of dehydration and anaemia.

"Parenteral diarrhoea" is given a definite place in the classification of infantile diarrhoea and vomiting in all paediatric textbooks, where it is usually stated that the gastro-intestinal symptoms are secondary to systemic or localized infection, and that they tend to clear up as soon as the parenteral cause is removed. The primary infection may be of virus, bacterial, or perhaps combined origin, and may be of surprisingly trivial nature. It is, however, well known that not all babies react thus to minor infections; and therefore, while accepting the role of the parenteral infection as an inciting agent in most of our cases, we feel that a greater tendency to respond to such stimuli by severe gastro-intestinal symptoms must be postulated in individual babies. Quite often the whole clinical picture is most suggestive of an upset caused by some "trigger" mechanism setting up the disproportionately violent reaction of diarrhoea and vomiting which eventually marches on its own way to a fatal outcome, regardless of the triviality of the first provoking factor. Here, certainly, death is due, not to infection, but to profound irreversible changes in the body chemistry.

Dehydration

The assessment of dehydration and degree of fluid loss is still based on subjective criteria and is often very difficult, especially in chubby, well-covered infants, in whom skin signs are absent or misleading. The need for a reliable laboratory or bedside test is great. Much excellent work has been done on the changes in body chemistry occurring in dehydration, in both adults and babies (Hoag and Marples, 1931; Aldridge, 1941). Most observers agree that the level of plasma chlorides and proteins in no way indicates the amount of fluid lost. The haematocrit and alkali-reserve determinations are considered more useful. In a few severely dehydrated infants in this series, all over 2 months of age, the haematocrit readings on admission ranged from 27 to 41 (average 36), obviously not confirming the clinical picture of severe fluid loss. When water balance had been restored, most of these infants were found to have a considerable degree of anaemia, which would account for the apparent absence of haemoconcentration. The accepted normal figure for the haematocrit in babies is 42, but Aldridge states that in infants of 2 to 8 months the normal reading is less than 38.

The low alkali reserve, ranging from 40 to 61.5 c.cm. (average 50.4 c.cm.), was more in keeping with the clinical condition of these infants. Unfortunately, the estimation of alkali reserve is time-consuming, and cannot easily be performed in small laboratories.

A raised blood urea was the most constant finding in our cases, the figures ranging from 50 to 112 mg. per 100 c.cm. (average 76 mg.), and corresponding fairly closely with the clinical assessment of dehydration in the individual cases.

PLASMA PROTEINS

The normal figures for plasma proteins in babies given in the literature vary widely. Hickmans, Finch, and Tonks (1943) give readings of 6 to 7.4 g. per 100 c.cm. for normal infants over 10 weeks of age. They quote Kylin (1932) for figures ranging from 4.6 to 6.5 g. for babies under 2 years of age, and Rennie (1935) from 6.04 to 8.0 g. per 100 c.cm. for babies of 3 to 23 months. The plasma protein levels found on admission in 7 of our severely dehydrated infants ranged from 5.06 to 6.44 g. (average 5.7 g.). The ages of these infants ranged from 2 to 8 months, and the average duration of diarrhoea before admission was 5 days, and of vomiting 3.9 days. Plasma protein levels were estimated in 4 other babies, 3 of them premature infants who, 1 to 2 days after intravenous therapy had been stopped, developed oedema while still apparently insufficiently hydrated. These values were: 4.7, 5.85, 5.7, and 4.3 g. per 100 c.cm., or an average of 5.14 g. Marked improvement and disappearance of the oedema followed the intravenous transfusion of half-strength serum in 2 cases, and of blood and half-strength serum in the other 2.

It is not unreasonable to assume that there exists in these infants some degree of protein deficiency, due mainly to restricted intake in their diluted feeds, and impeded digestion

and absorption of feeds; there may also be loss of proteins through the damaged capillaries of the intestinal wall. Recent work has shown that premature infants usually have a lower plasma protein level than full-term babies. Hickmans, Finch, and Tonks (1943) found readings of 3.7 to 5.4 g. per 100 c.cm. in premature babies in the first four weeks of life. The deficiency may therefore be expected to be still more marked in premature infants with diarrhoea and vomiting, who probably also have a smaller store of proteins in their bodies.

Formerly, we had found the correction of fluid loss by crystalloid solutions very difficult in some cases; prematures, especially, often became oedematous before being fully hydrated. The early administration of diluted serum or plasma has been of real assistance in overcoming this difficulty, and also in restoring and maintaining the circulation in badly shocked cases. We noted one other effect of the injected plasma—namely, an early reduction in the size and frequency of large, watery stools.

DANGERS OF SERUM THERAPY

We wish to draw attention to the dangers of too enthusiastic serum therapy. During the course of intravenous therapy it was our custom to follow each vacoliter bottle of half-strength serum or plasma by a bottle of half-strength Hartmann's (Ringer-lactate) solution + 5% glucose. In 4 consecutive cases half-strength serum was infused continuously. Although the quantity of fluid given did not exceed the requirements for body weight (2½ oz. per lb. per day plus an allowance of 3 to 6% of body weight for dehydration), in less than 24 hours the children showed signs of respiratory embarrassment, marked cyanosis, rapid thready pulse, and anuria. No oedema was found. Two of these babies died of cardiac failure, and 2 recovered after the administration of diuretics and continuous oxygen, the intravenous drip being discontinued. It seemed that in these small infants the continuous infusion of proteins caused the tissue fluids to be drawn into the blood stream in order to lower the raised osmotic pressure of the circulating blood, and there to be retained, thus causing circulatory embarrassment.

Heyl and Janeway (1942) state that 1 g. of albumin, which is osmotically equivalent to 1.25 g. of plasma protein, attracts, on an average, 18 c.cm. of fluid into the circulation in one hour. Thus the danger of giving large quantities of undiluted plasma intravenously to dehydrated infants is obvious. Normally, the total quantity of protein which we gave intravenously in the first 48 hours of treatment to a baby weighing 10 lb. was approximately 15 g., the serum or plasma being diluted with Hartmann's solution. We are unable to say how much of this injected protein was actually metabolized by the body; but it is our impression that the plasma helped to restore the water balance more quickly and with greater safety, and to maintain it until the infant was able to take full feeds.

LIVER CHANGES

We would like to make a plea for further research into the origin of the fatty liver so often found at necropsy on cases of protracted diarrhoea and vomiting. Macro- and microscopical evidence of liver damage was found in 6 of our babies on whom post-mortems were performed, in extreme degree in 2 of them. Lately, a good deal of work has been done on diets producing and preventing liver damage (Ravdin *et al.*, 1943; Himsworth and Glynn, 1944). Although various other factors probably cause the initial toxic changes in the livers of babies suffering from diarrhoea and vomiting (e.g., infection), it seems to us that the extreme fatty infiltration often found after death may be at least partly due to protein starvation, especially lack of some of the important amino acids. These children often live for weeks on diluted "milk formulas," the digestion of which is further impeded by diarrhoea and persistent vomiting. We have often witnessed in these babies what, in an adult case, would have been called a death from liver insufficiency. This, according to personal communication, has also been the impression of other workers. Some of these infants did not appear at all cachectic even at necropsy, and yet the condition of their livers was clearly incompatible with life.

This applies equally to the plump, apparently slowly recovering babies, who when stricken down with a new infection very often have an alarmingly severe relapse, frequently fatal. The severity of the second attack is usually ascribed to a reinfection with a more virulent form of gastro-enteritis. We feel that due attention should be paid to the possibility that these children, although outwardly in good condition, may not yet have repaired the liver damage caused by the first attack and possibly accentuated by weeks of careful but very deficient feeding. The inability of patients with damaged livers to stand up to even minor infections is well known, and this should be borne in mind before postulating increased virulence of the second attack.

Relapse

As has been said above, there were 27 relapses in this series (19.3% of all cases), and 6 of these patients died. The relapses were commonly more severe than the primary attack. In 19 cases (70.4%) the relapse was preceded by pyrexia and clinical signs of parenteral infection.

Approximately half the infants (73) were nursed in cell wards; among these there were 6 relapses, or 8.2%, and 1 died. The remaining 67 infants were nursed in a 20-bedded "barrier" ward, with the same routine of management and treatment; here there were 21 relapses (31%), with 5 deaths. The highest relapse rate occurred during a period when the number of bottle babies in the barrier ward reached 16. Nursing in barrier wards, therefore, however strictly the rules of bed-isolation are observed, does not appear to be as effective as cell or single-bedded-ward nursing in the prevention of cross-infection.

Haematology

In a number of cases, especially those in which a mastoiditis was suspected, total and differential white cell counts were made, but the results were inconclusive; this was possibly partly due to intensive sulphonamide therapy.

Haemoglobin estimations in some of the severely dehydrated infants were made on admission. Here again the findings were not helpful in the assessment of dehydration. Haemoglobin values (Sahli) ranged from 70 to 90% (average 80%), and did not confirm the clinical evidence of severe fluid loss and shock. In several of these cases an underlying, often severe, anaemia became apparent when fluid loss had been corrected. Haemoglobin estimations in 30 infants who, though no longer dehydrated, were not making satisfactory progress showed values of 100% in only 2 cases. In the remaining 28, investigated between 5 and 37 days after admission, haemoglobin values ranged from 42 to 88% (average 60%). These low haemoglobin levels appeared to be due to a multiplicity of causes, singly or in combination: (1) Previous microcytic anaemia, especially in the premature babies. (2) Effect of intensive sulphonamide therapy, although this was usually well tolerated. (3) Insufficient intake of food during the illness and convalescence. (4) Insufficient absorption of food, vitamins, and administered iron, due to changes in the intestinal mucosa even after cessation of diarrhoea. (5) Parenteral infection.

We found that the routine administration of iron, in the form of a ferrous sulphate mixture, combined with liberal allowances of vitamins, did much to accelerate convalescence and recovery. Infants showing haemoglobin values below 60% were given transfusions of 200 to 300 c.cm. of blood, often with dramatic improvement.

Treatment

This, as previously described (Alexander and Eiser, 1943), was based on the following principles:

1. The search for, and elimination of, foci of parenteral infection. Sulphonamides, chiefly sulphathiazole, were given in large doses (3 to 4½ g. daily for 5 to 7 days), and operative measures undertaken as required.

2. The adequate administration of fluids and food to meet the infant's daily requirements and to prevent the onset of dehydration, and as early a return to full-strength feeds as the infant would tolerate. On admission they were given half-strength Hartmann's solution by mouth for 12 to 24 hours. If vomiting had ceased, dilute milk feeds, 1:8 or 1:6 were then begun, and the strength of the feeds was gradually increased until the infant was taking a full-strength milk-feed, usually in 4 to 7 days. If vomiting persisted, all feeds were stopped and fluids were given parenterally. It

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

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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;