Our range of M.C.D. was from 5.944 to 7.642 μ . Price-Jones gives the normal range of M.C.D. for non-pregnant women as 6.686 to 7.718 μ . Elliott (1944), who presents the only other published series of observations on M.C.D. in pregnant women with a haemoglobin of 11 g. per 100 ml. or more, measured the M.C.D. in 14 cases and found it to be between 6.7 and 7.7 μ . In none of our cases did there seem to be any degree of correlation between the M.C.V. and M.C.D. confirming the findings of Mogenson (1938), Schalm (1939-40), and Elliott (1944). In eight of our cases the M.C.D. was below Price-Jones's normal range on two or more occasions, and in one (Case 7) it was consistently below throughout pregnancy, despite the fact that her haemoglobin level, red cell count, and M.C.V. were well within normal limits throughout. Case 12 has not been included in the above eight because her haemoglobin began to fall after the sixth month and she was treated as a case of iron-deficiency anaemia; her M.C.D. fell below Price-Jones's normal range from the sixth month onwards.

Although there are statistically significant differences in the M.C.D. from month to month in the same individual pregnancy, these are found irregularly, and there seems to be no consistent tendency for the M.C.D. to increase or decrease significantly as pregnancy advances.

The variability percentage of the M.C.D. is usually taken as a statistical expression of the degree of anisocytosis. The upper limit of normal established by Price-Jones (1933) for healthy adults of both sexes is 7.3%. Our figures range from 5.87% to 9.86% and lie above 7.3% in 54 out of our 95 observations (56.7%). In no case was the variability percentage normal throughout pregnancy. There was no particular trend with regard to the variability percentage, abnormal findings being scattered throughout pregnancy.

Discussion

We believe that these are the first published observations on M.C.D. made serially on normal women throughout pregnancy. The analysis of our results shows that the M.C.D. of the red cells in pregnancy varies over a much wider range than in the non-pregnant individual. No fewer than 10 of our patients showed an M.C.D. of less than 6.686 μ (the lowest limit of normal given by Price-Jones) at one or more monthly examinations. In no case was it higher than normal. There is a definite tendency to increased anisocytosis in pregnancy even though the haemoglobin, red cell count, and M.C.V. are normal. There does not seem to be any correlation between abnormal microcytosis and anisocytosis. It is of interest to note that of Elliott's 20 normal patients 11 showed excessive anisocytosis.

Boycott (1936) has suggested that an abnormal degree of anisocytosis is a more important sign of abnormal haemopoiesis than any fall in haemoglobin level. If this is true our findings suggest that abnormal haemopoiesis is a feature of normal pregnancy. Since the M.C.D. tends to be low it is tempting to ascribe this to a dietary deficiency of iron. Moreover, Fullerton (1936) has calculated that the extra requirement of iron by the pregnant woman is not less than 2 mg. daily, and McCance *et al.* (1938) concluded that a satisfactory daily intake of iron during pregnancy would be 20 mg., an amount far higher than is usually supplied in most working-class or middle-class diets to-day. A dietary deficiency of protein might produce changes in the peripheral blood simulating an iron-deficiency anaemia.

Moreover, clinical experience shows that in pregnancy an anaemia which has all the features of iron deficiency in the peripheral blood can be associated with a megaloblastic

marrow reaction, and that this type of anaemia responds not to iron but to liver extract. It seems possible that the low M.C.D. associated with evidence of increased anisocytosis in pregnancy indicates a relative dietary deficiency, and that the increased stress of producing the material for the foetal red cells is shown in the altered architecture of the maternal erythrocytes—namely, a tendency to low M.C.D. with increased anisocytosis.

Summary

Serial estimations of haemoglobin, red cell count, mean corpuscular diameter, and mean corpuscular volume have been made during pregnancy in 16 healthy women.

The M.C.D. shows a greater range of variation than in healthy non-pregnant women.

There is evidence of abnormal haemopoiesis, indicating that a woman's diet is not completely adequate to supply the needs of both her own and the foetal red cells.

REFERENCES

- Adair, F. L., Dieckmann, W. J., and Grant, K. (1936). *Amer. J. Obstet. Gynec.*, **32**, 560.
 Bethell, F. H. (1936). *J. Amer. med. Ass.*, **107**, 564.
 Boycott, J. A. (1936). *Lancet*, **1**, 1165.
 Clegg, J. W., and King, E. J. (1942). *British Medical Journal*, **2**, 329.
 Dieckmann, W. J., and Wegner, C. R. (1934). *Arch. intern. Med.*, **53**, 345.
 Elliott, G. A. (1944). *J. Obstet. Gynaec. Brit. Emp.*, **51**, 198.
 Fullerton, H. W. (1936). *British Medical Journal*, **2**, 523.
 McCance, R. A., Widdowson, E. M., and Verdon-Roe, C. M. (1938). *J. Hyg., Camb.*, **38**, 596.
 Miller, H. G., and Studdert, T. C. (1942). *Lancet*, **2**, 332.
 Mogenson, E. (1938). *Studies on the Size of Red Blood Cells*. Munksgaard, Copenhagen.
 Price-Jones, C. (1933). *Red Blood Cell Diameters*. Oxford University Press, London.
 Schalm, L. (1939-40). *Folia haemat., Lpg.*, **63**, 34.
 Strauss, M. B., and Castle, W. B. (1932). *Amer. J. med. Sci.*, **184**, 663.
 Watson, H. G. (1938). *Amer. J. Obstet. Gynec.*, **35**, 106.
 Wintrobe, M. M., and Shumacker, H. B. (1935). *J. clin. Invest.*, **14**, 837.
 — *et al.* (1937). *Amer. J. med. Sci.*, **193**, 449.

DIRECT MICROSCOPICAL EXAMINATION OF FAECES IN INFANTS

BY

CONSTANCE A. C. ROSS, M.D.

(From the University and Knightswood Hospital, Glasgow)

The direct microscopical examination of a film of faeces has one great advantage over study of faeces by selective cultural media in that it affords a representative picture of the intestinal flora as a whole. The purpose of the present report is to record the results of such an examination of the faeces of infants both in health and in disease.

This investigation originated from a study of the problem of gastro-enteritis in infancy, of which an outstanding feature is its much greater frequency in artificially fed infants than in the breast-fed. Moreover, it has been shown by various workers that breast-fed infants have a decided advantage over bottle-fed infants in their resistance to infections of various kinds (Grulee, Sanford, and Herron, 1934; Cordua, 1935; Levi, 1941). During the past fifty years various attempts have been made to discover if any fundamental difference existed between the breast-fed and the artificially fed infant which might predispose the latter to infection, and especially to gastro-enteritis. In particular, the faeces have been extensively studied ever since Tissier, in 1900, demonstrated the pronounced difference between the intestinal flora of the suckling and the bottle-fed infant.

We have found that direct microscopical examination of a thin smear of faeces, stained by Gram's method, reveals certain striking features not only in the intestinal flora of the healthy breast-fed infant and the healthy artificially fed infant but also in infants suffering from "gastro-enteritis."

The Intestinal Flora of Healthy Infants

A film of faeces from a breast-fed infant presents a characteristic picture. The predominant organism—a thin Gram-positive bacillus—comprises almost 100% of the flora. Tissier first described this organism and named it *Bacillus bifidus communis*—later workers placed it in the lactic-acid group of bacilli. Cruickshank (1925) made a careful study of the morphology and cultural characteristics. It is a thin straight or slightly curved bacillus of variable length, with round or pointed extremities, sometimes arranged in pairs with one end touching, sometimes in groups of bacilli lying parallel to one another. The microscopical picture of a film of faeces from an artificially fed infant is very different. There is no predominant organism. About 50% of the flora consists of Gram-positive organisms, the majority of these being lanceolate cocco-bacilli arranged singly or in pairs. In addition, non-bacterial faecal material is much more abundant than in the breast-fed infant's stool, and is especially so in faeces from infants receiving raw cows' milk.

We have confirmed these findings in a group of healthy infants under 6 months of age attending various child-welfare clinics in Glasgow. Specimens of faeces from 52 breast-fed infants were examined. In 49 cases a direct film showed that the lactobacilli comprised 75 to 100% of the total intestinal flora. The three infants in whom the direct smear showed less than 50% lactobacilli were below 1 month old and were all underweight. This suggests that these babies were not receiving an adequate supply of breast milk.

In order to find out at what period after birth the *Lactobacillus bifidus* gains predominance in the intestinal flora, specimens of faeces from 38 newly born infants (aged a few hours to 14 days) were examined. It is evident from Table I that for the first 48 hours after birth the faeces often show no bacterial flora. However, in all the breast-fed infants over 6 days old the lactobacillus was found to be the predominant organism.

In contrast with these findings in breast-fed babies, Table II shows that in a large proportion of the specimens of faeces from 46 artificially fed infants lactobacilli were scanty or absent. (By far the greatest proportion of these

TABLE I.—*Lactobacilli in Faeces of Breast-fed Infants from Birth to 14 Days*

	0-2 Days	3-6 Days	7-10 Days	11-14 Days	Total
Lactobacilli over 50%..	3	11	9	3	26
Lactobacilli 10-50%..	2	5	—	—	7
No organisms present	5	—	—	—	5
Total	10	16	9	3	38

TABLE II.—*Lactobacilli in Faeces of Artificially Fed Infants*

	2 Weeks-1 Month	1-2 Months	2-3 Months	3-4 Months	4-5 Months	5-6 Months	Total
Lactobacilli over 50%..	—	1	—	—	1	—	2
Lactobacilli 10-50%..	—	3	3	3	1	1	11
Lactobacilli scanty or absent ..	1	15	—	9	5	3	33
Total	1	19	3	12	7	4	46

infants were receiving National Dried Milk, a few were being fed on diluted cows' milk, and two infants were on a proprietary milk.)

Microscopical Examination of Faeces in Infants with "Gastro-enteritis"

The diagnosis of gastro-enteritis in infancy comprises a wide variety of upsets, which are generally placed in one of the following three groups: (a) dietetic diarrhoea; (b) diarrhoea due to a parenteral infection; and (c) true gastro-enteritis, in which no apparent cause for the diarrhoea can be discovered. The distinction between these three groups is by no means absolute: an infant who appears to have a mild dietetic diarrhoea on admission may become badly dehydrated and run the course of a true gastro-enteritis. A direct film of the faeces of 75 infants admitted to the ward with the diagnosis of "gastro-enteritis" showed certain interesting features. The patients were placed in

TABLE III.—*Gram-positive Organisms on Admission Film, and Type of Enteritis*

	Gram-positive Organisms				Total Cases
	±	+	++	+++	
Dietetic diarrhoea	—	2	7	14	23
Parenteral infection present ..	4 (1)	11 (1)	9	11	35 (2)
True gastro-enteritis	9	8 (3)	—	—	17 (3)
Total	13 (1)	21 (4)	16	25	75 (5)

(Figures in parentheses indicate deaths)

± = scanty. ++ = 25-50% of total flora.
+ = less than 25% of total flora. +++ = over 50% of total flora.

one of the three groups described, in accordance with the clinical history and clinical signs. The faecal smears were examined without consideration of the clinical findings. In view of the obvious difficulty of conducting an actual bacterial count, the proportion of Gram-positive organisms in the smear was estimated in four rough categories as shown in Table III.

It will be seen from Table III that in the majority of cases of dietetic diarrhoea the intestinal flora showed Gram-positive organisms in the "normal" proportion for artificially fed infants. This was in marked contrast to the microscopical picture presented by the specimens from infants suffering from true gastro-enteritis. In this group the proportion of Gram-positive organisms never rose above 25% of the total flora, and in 9 of the 17 cases the Gram-positive organisms were scanty.

It may be that any severe diarrhoea will itself cause a shift towards a Gram-negative flora. Such a view finds support from the fact that in the group of dietetic cases the diarrhoea was mild and short-lived and clinical signs of dehydration were usually absent, whereas in the true gastro-enteritis group the diarrhoea was moderate or severe and there was always some degree of dehydration present. In those cases with parenteral infections the severity of the diarrhoea and dehydration varied considerably, and, as seen from Table III, the proportion of Gram-positive organisms was also very variable. Some of our gastro-enteritis cases were treated with oral aerosporon or streptomycin. These antibiotics destroyed the Gram-negative organisms in the intestinal flora, gradually producing a completely Gram-positive picture. Direct smears taken during treatment with aerosporon or streptomycin were thus of little value. However, of the patients who died, two infants suffering from true gastro-enteritis received no chemotherapy, and it was of interest to note that their faecal smears showed a progressive decrease in Gram-positive organisms until, prior to death, the flora was almost completely Gram-negative.

Discussion

These results are considered to be worth recording in view of the findings of McFarlan, Crone, and Tee (1949). These workers studied the flora of the throat and rectum of infants in two maternity units, by cultural methods and by direct microscopical examination. They found a higher incidence of coliform bacilli in the artificially fed infants than in the breast-fed infants, and suggested that their methods might be applied to the investigation of neonatal diarrhoea. As a result of the present investigation we feel that, in babies suffering from enteritis, the direct microscopical examination of a film of faeces is of considerable value. A marked shift towards a Gram-negative flora is likely to indicate a severe degree of enteritis, probably with a bad prognosis. It cannot yet be decided whether a Gram-negative flora is the result of increased intestinal hurry or whether proliferation of Gram-negative organisms initiates diarrhoea.

The present study demonstrates the pronounced difference between the intestinal flora of the healthy breast-fed infant, the healthy bottle-fed infant, and the infant acutely ill with gastro-enteritis. Within recent years much work has been done on the synthesis of nutrients by intestinal organisms, and one would imagine that the nutrients synthesized by the lactobacillary flora would be very different from those synthesized by the heterogeneous flora found in the infant receiving artificial feeds. Moreover, the relative absence of lactobacilli from the stools of artificially fed infants might indicate a deficiency of certain factors in cows' milk which are perhaps essential not only for the growth of these organisms but also for the infant's adequate nutrition and resistance to infection.

Summary

Direct microscopical examination of faecal smears was made in 52 breast-fed infants. In 49 cases *Lactobacillus bifidus* was the predominant organism. Of direct smears from 46 artificially fed infants lactobacilli were scanty or absent in 33.

In faecal smears from 38 newly born infants the lactobacillus was predominant in all those over 6 days old.

Of 75 infants admitted to hospital with the diagnosis of enteritis, those showing a large proportion of Gram-negative organisms in their faecal smears were severely ill.

The possible relationship of the intestinal flora to the infant's health is discussed.

This investigation has been carried out under a grant from the Scientific Advisory Committee. I wish to thank Dr. T. Anderson for his constant guidance and for his help with the manuscript of this article.

REFERENCES

- Cordua, O. B. (1935). *Arch. Pediat.*, **52**, 845.
Cruickshank, R. (1925). *J. Hyg., Camb.*, **24**, 241.
Grulec, C. G., Sanford, H. N., and Herron, P. H. (1934). *J. Amer. med. Ass.*, **103**, 735.
Levi, D. (1941). *British Medical Journal*, **1**, 963.
McFarlan, A. M., Crone, P. B., and Tee, G. H. (1949). *Ibid.*, **2**, 1140.
Tissier, H. (1900). *La Flore Intestinale des Nourrissons*. Paris.

The Ministry of Health has issued a revised edition of a booklet which originally appeared in 1942 on "The Feeding of Children from One to Five Years" (H.M.S.O., 6d.). It is intended mainly to advise on the feeding of groups of pre-school children in nurseries and elsewhere, but it may also be of help to individual parents and guardians. The normal and priority rations available to children are listed, and the booklet includes a number of useful recipes. The last section gives some homely advice on educating the child in sound feeding habits, making the point that the food should be attractive and varied, and served in as pleasant surroundings as possible.

CHLORAMPHENICOL AND THE VENEREAL DISEASES

BY

R. R. WILLCOX, M.B., B.S.

Physician in Charge, V.D. Department, King Edward VII Hospital, Windsor; Consultant in Venereology, St. Mary's Hospital, London

"Chloromycetin," which is prepared from the cultures of *Streptomyces venezuelae*, has been synthesized and given the name chloramphenicol. It is supplied in capsules of 0.25 g. for oral use. Apart from its important effects upon the organisms of typhus and typhoid fevers, undulant fever, and primary atypical pneumonia, as has "aureomycin," it has considerable application in the field of venereology, for it has some action on most of the known venereal diseases.

The following case reports indicate that it is effective to some extent on the organisms of syphilis, gonorrhoea, and soft sore (chancroid).

Case 1: Sero-negative Primary Syphilis

A young male native from Nyasaland reported on September 30, 1949, with an indurated chancre of the prepuce and typical bilateral syphilitic inguinal glands. He had had the lesions for fourteen days, having contracted the disease two weeks previously. *Treponema pallidum* was found without difficulty, but the serum Wassermann reaction was negative. He was given three 0.25-g. capsules of chloramphenicol on the first day, and thereafter two capsules a day until he had had eleven in all (total, 2.75 g.). Although the dark field was still positive at 24 hours and again at 48 hours, it was negative at 72, 96, and 120 hours, and by the sixth day the sore had healed.

Case 2: Sero-positive Primary Syphilis

A male native of Southern Rhodesia had an indurated sore in the coronal sulcus of seven days' duration, and the left inguinal glands were enlarged and tender. *T. pallidum* was seen in the dark field and the Wassermann reaction of the blood was strongly positive. His most recent exposure to infection was only ten days previously, and it was considered likely that a chancroid infection had been superadded.

He was given three 0.25-g. capsules of chloramphenicol on the first day and subsequently one capsule twice a day to a total of seven (1.75 g.). The dark field was negative at 24 hours and again 48 hours after the onset of treatment, but by the third day the sore had healed. Meanwhile the inguinal glands had lost their tenderness within 24 hours.

Case 3: Secondary Syphilis

A young adult male native of Southern Rhodesia attended with scrotal ulceration and typical condylomata lata around the anus with mucous patches on the buccal mucous membrane, lips, and tongue. The dark field was teeming with *T. pallidum* and the Wassermann reaction of the blood was strongly positive. He was given three 0.25-g. capsules of chloramphenicol on the first day, followed by one capsule twice a day to a total of twelve (3 g.). The dark field was negative at 24 hours and the lesions had all healed by the ninth day. When he was used for demonstration purposes at a medical meeting on the eleventh day nothing abnormal was to be seen.

Case 4: Secondary Syphilis

Another male native of Southern Rhodesia also had obvious lesions of secondary syphilis with hypertrophic condylomata lata on the penis, scrotum, around the anus, and on the inner thighs. There was also a large papular rash. *T. pallidum* was readily seen in the dark field, and the Wassermann reaction was strongly positive.