SKIMMED MILK AND KWASHIORKOR

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An investigation to determine the precise factors in skimmed milk which are responsible for initiating the cure of kwashiorkor has been reported elsewhere.[4] As part of this investigation a series of cases were treated with skimmed milk, some with and some without a vitamin supplement. It was shown that the vitamin supplement made no significant difference to the rate of cure. In a limited number of cases an imported dried skimmed milk appeared to be superior to the locally-made product.

To clarify this observation a larger number of cases has now been brought into each series. In addition a further group has been treated with fresh skimmed milk containing a protein and vitamin supplement.

In this communication we refer to the relative effectiveness of these 4 skimmed-milk formulae in the initiation of cure of this syndrome.

Case Material and Methods. Criteria of selection and methods were identical to those described previously.[4] The composition of the test feeds is shown in Table I.

TABLE I. COMPOSITION AND CODE NUMBERS OF TEST FORMULAE

SADM. South African dried skimmed milk (roller dried) with no vitamin supplement.

SADM+VS. The same South African dried skimmed milk with daily vitamin supplement of:

Thiamine	4-6 mg.
Nicotinic acid	30-45 mg.
Riboflavine	3·4-4·4 mg.
Pyridoxine	4 micrograms
Calcium pantothenate	0·25-1 mg.
Vitamin B_{12}	6 micrograms
Vitamin A	6,000 units
Vitamin D	1,600 units
Ascorbic acid	80-105 mg.
Folic acid	5 mg.

In Pretoria 1½ minims of 85% lactic acid per fl. oz. was added to these skimmed-milk mixtures.

Imported milk. Imported spray-dried skimmed lactic-acid milk with total acidity of 5% and without vitamin supplement.

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Pretoria routine treatment

1. *Formula*

Fresh skimmed milk	2½ oz/lb/24 hours (usually 40-50 oz.)
Dextrimaltose	5% (usually 2-2½oz.)
Calcium caseinate	2½% (usually 1-1¼ oz.)

Lactic acid 85%, 1½ minim per oz. of milk.

2. *Liver extract:* 1 ml. intramuscularly daily for the first 7 days and from then onwards 1 ml. 3 times weekly.

3. *Lipotropic factors:* The patients received daily a supplement containing:

Liver concentrate	300 mg.
Choline chloride	0·8 g.
Methionine d.l	0·68 g.
Inositol	0·5 g.

4. *Vitamin supplement:* This was given from the beginning of the 2nd week onwards and in the following daily quantity.

Vitamin A	9,000 units
Vitamin D	2,400 units
Thiamine	4·5 mg.
Riboflavine	3·6 mg.
Ascorbic acid	120 mg.
Nicotinamide	30 mg.
Vitamin B_{12}	15 micrograms
Folic acid	5 mg.

5. Ward diet was introduced gradually from the beginning of the 2nd week. If indicated 2 gr. of ferrous sulphate *t.i.d.* was prescribed at this stage.

During the first 12-24 hours all cases received an electrolyte solution such as Darrow's or Hartman's for correction of dehydration and to serve as a period of observation before the milk formulae were introduced. The two brands of dried milk were prepared to provide 5-10 calories per fl. oz. The fluid intake prescribed was approximately 2½ oz. per lb. per 24 hrs. With improvement of appetite the strength of the feed was increased to 15 calories per fl. oz. (1½ oz. dried milk per 10 oz. of water) and total fluid intake adjusted to the infant's demand. The fresh skimmed-milk mixture provided approximately 18 calories per fl. oz. It was rarely necessary to dilute this mixture as it was well tolerated in full strength. Procaine penicillin, 300,000 units daily by intramuscular injection, and oral sulphadiazine, 1½ gr. per lb. body-weight daily, was administered to all cases for at least a week.

Criteria of cure. The results are concerned with initiation of cure only, as previously defined.[4] In summary it can be said to have taken place when the previously downhill course of the disease has been changed into an upward one, usually within a period of 12-24 days. By this time the skin lesions are healing and the patient has lost his oedema and he has become interested in his surroundings and regained his appetite. Objectively the serum albumin will have shown a rapid rise. At this stage cure can be said to have been initiated and the therapeutic tests end. The introduction of mixed feeds is now necessary to satisfy appetite, to promote growth and development, and to consolidate cure.

RESULTS

The results have been arranged as follows:

Group 1 are the cases in which no treatment was given other than that laid down as a standard for all, and in which cure was fully initiated within 21 days.

Group 2 are cases in which the same end-result was achieved only with the aid of additional antibiotic therapy in the form of terramycin, aureomycin or chloramphenicol.

Group 3 are cases in which additional supportive transfusion of plasma or blood was necessary to initiate cure.

Group 4 are the deaths, including those occurring within 48 hours.

In Table II the results have been set out according to the above grouping. To overcome the variables of supportive treatment and to facilitate statistical analysis a simplified form of grouping has been adopted for the cases treated in Pretoria (Table III). In this all cases not classed as a group-1 cure have been regarded as failures. In this way it is possible to examine the ability of a formula to initiate cure in the absence of any supportive treatment other than penicillin and sulphadiazine.

TABLE III. STATISTICAL ANALYSIS OF RESULTS FROM PRETORIA

Formula	*Group* 1	*Groups* 2, 3, 4 (*Failure*)	*Total*
SADM+VS (skimmed milk with vitamin supplement) ..	28 (69%)	14	42
SADM (skimmed milk without vitamin supplement) ..	23 (57·5%)	17	40
Borden's skimmed lactic-acid milk	22 (92%)	2	24
Pretoria routine treatment ..	27 (66%)	14	41

Analysis by X^2

SADM+VS/SADM/Borden's/Pretoria routine $0{\cdot}05>P>0{\cdot}02$ Significant

SADM+VS/SADM/Pretoria routine $0{\cdot}7>P>0{\cdot}5$ Not significant.

SADM+VS/Borden's $0{\cdot}05>P>0{\cdot}02$ Significant.

Using the same grouping for the combined results of the two centres the significant tests are:

SADM+VS/SADM/Borden's $P>0{\cdot}01$ Significant

SADM+VS/SADM $0{\cdot}2>P>0{\cdot}1$ Not significant.

From the data it can be seen that satisfactory initiation of cure was achieved with all the 4 formulae used. The imported skimmed lactic-acid milk without any supplementation gave significantly better results (88% cure for the whole series, 92% cure for the Pretoria cases) than the other 3 formulae, which were made up with South African skimmed milk (see bottom of Table III for X^2 analysis).

The differences in cure rate between these latter 3 formulae proved to be not significant. This confirms our previous findings[4] that the addition of vitamins to a basic milk-formula does not significantly improve the cure rate. The same may now be said for the addition of a casein, dextrimaltose and vitamin supplement (the Pretoria routine treatment.)

The rate of rise of serum albumin in the series treated with the imported skimmed lactic-acid milk is shown in Fig. 1 and compared with that previously obtained with the South African skimmed-milk formulae.[4] There is no significant difference in the steepness of the regres-

TABLE II. DETAILED ANALYSIS OF RESULTS

Formula	*Centre*	*No. of cases*	*Group* 1	*Group* 2	*Group* 3	*Group* 4	
						Total	48-*hour deaths excluded*
SADM+VS (Skimmed milk with vitamin supplement	Pretoria	42	28	2	8	4	2
	Cape Town	7	3	2	1	1	1
	Total	49	31 (63%)	4	9	5	3
SADM (skimmed milk without vitamin supplement	Pretoria	40	23	0	9	8	5
	Cape Town	12	2	4	2	4	2
	Total	52	25 (48%)	4	11	12	7
Borden's skimmed lactic-acid milk	Pretoria	24	22	0	0	2	2
	Cape Town	10	8	1	0	1	0
	Total	34	30 (88%)	1	0	3	2
Pretoria routine treatment	Pretoria	41	27	2	5	7	4
	Total	41	27 (66%)	2	5	7	4

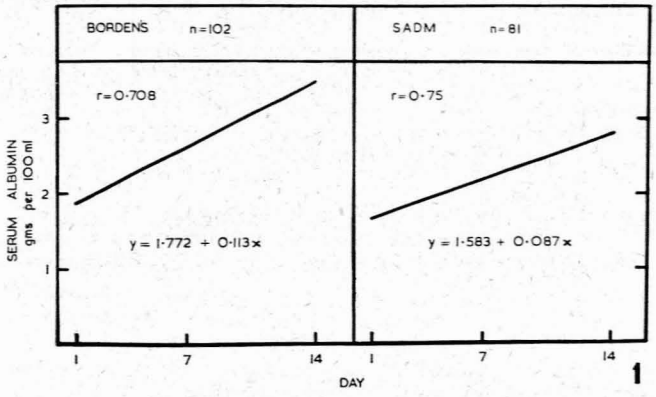

Fig. 1. Regression lines of rise of serum-albumin (Y) against time (X) during treatment with imported spray-dried acidified skimmed milk and South African skimmed milk (roller dried).

sion slope obtained with the two types of formula. Thus although clinically the cases on the proprietary formula did better the rate of recovery as judged by return of serum albumin to normal levels was in no way different.

DISCUSSION

The introduction of skimmed milk in the treatment of kwashiorkor has been a considerable therapeutic advance.[1, 3, 15, 16] It is now generally regarded as the dietary therapy of choice in this syndrome. There is, on the other hand, some divergence of opinion on whether the addition of vitamin or protein supplements is desirable.[5, 6, 7, 8, 10, 11, 12, 14, 15, 16]

Our results here confirm previous observations by ourselves and others that a vitamin supplement does not significantly alter the rate of initiation of cure. A similar conclusion can now be drawn about the addition of protein to a basic skimmed-milk formula. These findings are based on the use of both fresh skimmed milk and locally produced dried preparations.

The superior results achieved with an unsupplemented imported brand of skimmed milk were unexpected and require fuller investigation. There are several possible explanations. The local dried milk was manufactured by the roller process. The imported variety is spray-dried, and this is generally considered to be a preferable method, expecially from the point of view of preservation of amino acids.[13a,13b] Packaging and storage of dried milk is of great importance. It has been shown that heat and humidity cause rapid deterioration of dried milk due to the so-called Maillard reaction.[9] In this reaction lysine and possibly some other amino acids become inactivated. The South African skimmed milk was supplied in bags that were not entirely impervious to moisture and it is possible that some change of this nature took place. On the other hand the imported milk was supplied in air-proof and moisture-proof containers. Lactic acid was added during manufacture of the imported milk whereas with the local dried milk lactic acid was added during preparation of feeds.

The form of testing employed in this investigation, i.e. a therapeutic trial, has its limitations in a syndrome such as kwashiorkor unless very large numbers of cases are employed. Response to treatment must depend on severity of illness. We have found it extremely difficult to establish definite criteria of severity and cannot fully exclude the possibility that the cases on the imported milk were in some indefinable way less severe than the other groups. Over half the cases on this milk were treated during the winter months of July and August—a period when gastro-enteritis is not a problem. This in itself may account for the better performance. On the other hand, with this preparation results were uniformly good in all centres, each case satisfied criteria of diagnosis, and objectively there was no difference in the degree of hypo-albuminaemia on admission. It is desirable that a larger number of cases be studied to confirm or disprove our findings.

An immediate practical implication is that high standards of preparation, packaging and storage are obligatory if widespread distribution of skimmed milk is to be fully effective in the prevention and cure of kwashiorkor.

SUMMARY

A dietary therapeutic trial of skimmed milk in cases of kwashiorkor is described. Skimmed milk is confirmed as being probably the best treatment for kwashiorkor. Vitamin or protein supplements added to skimmed milk do not increase its efficiency in the initiation of cure. High standards of preparation and packaging of dried-milk products appear to be of more importance as judged by superior results obtained with an imported brand of dried skimmed milk.

OPSOMMING

'n Ondersoek waar gepoog is om die terapeutiese invloed van afgeroomde melk op die genesing van pasiënte met kwashiorkor vas te stel is beskryf. Daar is bevestig dat afgeroomde melk waarskynlik die beste voeding vir gevalle van kwashiorkor is. Byvoeging van vitamiene of proteïene by afgeroomde melk het nie die doeltreffendheid daarvan om die aanvang van genesing te bewerkstellig verhoog nie. Dit kom voor of hoë standaarde vir die vervaardiging en verpakking van melkpoeiers van meer belang is as daar gelet word op die beter resultate wat met die ingevoerde melkpoeier verkry is.

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REFERENCES

1. Altmann, A. (1948): Clin. Proc., **7**, 32.
2. *Idem* (1953): S. Afr. J. Clin. Sci., **4**, 71.
3. Brock, J. F. and Autret, M. (1952): *Kwashiorkor in Africa* Wld. Hlth. Org. Monogr. Ser. No. 8.

4. Brock, J. F., Hansen, J. D. L., Howe, E. E., Pretorius, P. J., Davel, J. G. A. and Hendrickse, R. G. (1955): Lancet, **2,** 355.
5. Clarke, M. (1951): E. Afr. Med. J., **28,** 229.
6. Frontali, G. (1954): Acta. paediat., **43,** suppl. 100, p. 318.
7. Gelfand, M. (1954): S. Afr. Med. J., **28,** 185.
8. Gillman, J. and Gillman, T. (1951): *Perspectives in Human Nutrition*, pp. 299-309. New York: Grune and Stratton.
9. Henry, K. M., Kon, S. K., Lea, C. H. and White, J. C. D. (1948): J. Dairy Res., **15,** 292.
10. Hughes, W. (1946): Trans Roy. Soc., Trop. Med. Hyg., **39,** 437.
11. *Idem* (1952): Brit. Med. J., **2,** 1,041.
12. Janssen, E. and le Roux, J. S. (1950): S. Afr. J. Clin. Sci., **1,** 100.
13. (*a*) Mrak, E. M. and Mackinney, G. in Jacobs, M.B., ed., (1951): *The Chemistry and Technology of Food and Food Products*, p. 1810. New York: Interscience Publishers Inc.
13. (*b*) Mauron, J., Mottu, F., Bujard, E. and Egli, R. H. (1955): Arch. Biochem. Biophys., **59,** 433.
14. Trowell, H. C. (1941-1942): Trans. Roy. Soc. Trop. Med. Hyg., **35,** 13.
15. Trowell, J. C., Davies, J. N. P. and Dean, R. F. A. (1954): *Kwashiorkor*, pp. 186-195. London: Arnold.
16. Walt, F., Wills, L. and Nightingale, R. P. (1950): S. Afr. Med. J., **24,** 920.