ing relative toxicity of old and freshly prepared quinine and aspirin mixture. The author replied that there is very little difference in the toxicity.

I. M. Kolthoff asked whether the color of the mixture changed more rapidly in the light than when kept in a dark place and whether a chemical change took place when the color darkened.

To the first question he replied that there seemed to be a variance and to the other that he did not go into the chemical examination of the mixture. In answer to a question by J. C. Munch, he replied that about one hundred frogs had been used in the experimentation, and at room temperature.

W. H. Zeigler said that clinically mixtures of quinine and aspirin had been found toxic, *i. e.*, reported so by physicians. He asked Dr. Ruddiman if he intended to continue the work and if so he hoped that warm-blooded animals would be used. The author replied that this was his intention. In his opinion the toxic symptoms induced by the mixture were due to the idiosyncrasy of persons to that mixture—there are persons who have an idiosyncrasy for quinine.

Various questions were asked relative to methods employed in mixing; to all of these the author replied and results are shown in the paper. Chairman Snyder hoped that experimentation with mixture on warm-blooded animals would be presented in a paper by the author next year, so that the question of toxicity of this mixture, which has been discussed for a number of years, may be settled.

MODIFICATION OF COW'S MILK FOR INFANT FEEDING.*

BY ELIZABETH GATES AND WYLY M. BILLING.

There will be no dispute of the statement that the best food for normal infants is human milk. This is an axiom with the medical profession. But in many cases human milk is not available, and the physician must do what he can with cow's milk, a food perfect for the calf, but very imperfectly adapted to the infant. Its chief disadvantages are (1) the difference in ratio of fats, carbohydrates and proteins from human milk, (2) its greater acidity, and (3) its tendency to form large indigestible curds in the stomach.

The percentage composition of human and cow's milk as taken from Thorpe[1] is as follows:

	Water.	Fat.	Sugar.	Casein.	Albumen.	Ash.
Cow's milk	87.25	3.75	4.75	3.00	0.40	0.75
Human milk	88.20	3.30	6.80	1.00	0.50	0.20

The most serious difference lies in the percentage of casein, which is the most difficult of the ingredients to digest. This difference is usually overcome by diluting the milk, the dilution varying with the age of the infant. The amount of sugar in cow's milk is low, so it is always necessary to add sugar, and even more necessary if the milk is diluted. If the fat percentage falls too low, it can be brought up by the addition of cream. Although the ash content of cow's milk is so much higher than that of human milk, there is some difference in the relative amounts of salts present. The following comparison, taken from Hess,[2] shows the difference in 100 parts of ash:

	K_2O.	Na_2O.	CaO.	MgO.	F_2O_3.	P_2O_5.	Cl.
Human milk	30.1	13.7	13.5	1.7	0.17	12.7	21.8
Cow's milk	22.14	15.9	20.05	2.63	0.04	24.7	21.27

According to this table, it can be seen that on dilution it is possible to reduce the amounts of potassium and sodium in cow's milk below that of human milk, and since these salts are very necessary, it would seem best, at least for diluted milk, to

* Scientific Section, A. Ph. A., Buffalo meeting, 1924.

add small quantities of sodium and potassium salts. An excess of salts does no harm because the surplus is not absorbed. Although the amount of iron in cow's milk is lower than that in human milk, neither kind of milk furnishes sufficient iron for the infant, so that for the first year it must draw upon the reserve of iron already stored in its body.

The second and third disadvantages of cow's milk, its acidity and its tendency to form large indigestible curds in the stomach, are often overcome simultaneously by the addition of bicarbonates, lime water, etc. Although these are expedients long familiar to every physician, it is only within the last few years that the theory of their action has been studied.

Comparative tests of cow's milk and human milk show that the curds from human milk are fine, flocculent and soft, so that they offer a maximum surface to the action of the digestive juices of the stomach with a minimum of resistance. On the other hand, the curds from cow's milk are quite large and tough, and are so hard that it is difficult for the gastric juices to penetrate them. Terry[3] has made an extensive study of milk curd formation and its modification. His conclusions, based on experiments *in vitro*, may be briefly summarized. The curd in milk results from the action of both rennin and calcium-ion on the caseinogen, the mother substance of casein. Rennin alone will not coagulate caseinogen, since it is a proteolytic enzyme, not a coagulating enzyme. The caseinogen is transformed by rennin to paracasein, which in the presence of calcium salts is insoluble, and precipitates out, in curds, as calcium paracaseinate. The curds of nascent calcium paracaseinate have a powerful coalescing property when just formed so that, if formed quickly, the small curds tend to coalesce into one or two large masses. However, this coalescing property is soon lost, so that if the curds are formed slowly no large proportion of them possesses this coalescing property at any one time, and the small curds remain distinct. Any substance or process which slows the formation of the curds will therefore cause them to be smaller and more digestible. The usual methods of milk modification are:

(1) Dilution with water
(2) Use of gruels and carbohydrates
(3) Boiling
(4) Use of citrates
(5) Use of alkalies

Since the dilution has to be governed by the amount of food which is needed by the infant and by the amount he is physically able to take care of, it is not often practical to dilute the milk enough to increase the time required for curding. Gruels modify the curds because of their protective colloidal action. Sugars do not affect the speed of curd formation appreciably, but do affect the quality of the curds. Of the three sugars, lactose, maltose and sucrose, lactose has the most favorable effect upon the curds. Boiling the milk modifies the curds, but it is open to the objection that it may also destroy the vitamins. Sodium citrate and the alkalies modify the curd formation because they withdraw some of the calcium-ion from the solution, thus reducing the proportions of one of the components of the reaction. For example, the action of sodium bicarbonate is

$$NaHCO_3 + Ca(H_2PO_4)_2 \longrightarrow CaHPO_4 + NaH_2PO_4 + H_2O + CO_2.$$

In this way the soluble primary calcium phosphate, of which cow's milk contains an excess, is converted into the insoluble secondary salt, thus withdrawing calcium-ion from solution. Lime water acts in a similar way because of its hydroxide radical and actually decreases the amount of calcium-ion present.

$$Ca(OH)_2 + Ca(H_2PO_4)_2 \longrightarrow 2CaHPO_4 + 2H_2O$$

Since cow's milk contains an excess of calcium salts, and since the large curds are caused to form by that excess, there is no justification for the addition of calcium salts to cow's milk. The addition of calcium salts is also not advisable because according to Bosworth,[4] "any increase in the amount of soluble calcium in milk also increases the possibility of the production of insoluble calcium soaps, which soaps may cause constipation." These soaps also withdraw needed fats from the metabolism.

It is interesting to note that several of Terry's observations as to the character of the curds formed by different modification methods were duplicated *in vivo* by Brenneman.[5] He "obtained the coöperation of a young adult who could empty the stomach of its contents by digital irritation of the fauces," and in this way was able to examine the stomach contents in their natural condition. His conclusions as to the type of curd produced by the various means of modification closely paralleled those of Terry.

From the above considerations it will be seen that an ideal milk modification mixture would satisfy the following requirements: (1) It should contain sugar to make up the deficiency in cow's milk; (2) it should contain salts to increase the sodium and potassium content; (3) it should partially neutralize the excess acidity, and (4) it should contain some milk curd modifier. Lactose should be used to supply the sugar deficit, since it gives the most desirable curds and has the advantage of a slight laxative action. Of the milk curd modifiers, sodium citrate, sodium bicarbonate and lime water seem to be the best. Lime water is the least practical of the three because so much of it has to be added to the milk. Sodium bicarbonate possesses the advantage over sodium citrate in that it also tends to neutralize the acidity. The addition of sodium bicarbonate and small amounts of sodium chloride and potassium bicarbonate also brings up the proportion of sodium and potassium in cow's milk.

EXPERIMENTAL STUDIES.

From a comparison of the analyses of cow's milk and that of human milk, it was ascertained that when one ounce of cow's milk was diluted with an equal volume of water it was necessary to add $17^1/_2$ grains of milk sugar in order to bring up the sugar content of the diluted milk to that of human milk.

Proceeding on this basis various other agents which are commonly employed in the modification of cow's milk were added in varying proportions. The effect of these combinations upon the length of time required for the curding of the milk and upon the character of the curd formed is shown in the tables given herewith.

The curding time recorded in the tables was determined in the following manner: Five cc. of rennin solution N. F. IV were added to four fluidounces of cow's milk which was maintained at body temperature (37.5° C.) until the curd formed separated from the walls of the container upon tilting. The time elapsing between the addition of the rennin and the formation of this curd is that recorded in the tables.

The relative toughness of the curds formed is indicated by the number of plus signs. These signs afford a rough estimate of the relative resistance to slicing by a glass stirring rod.

Tables II and III show the results obtained with other samples of whole milk of different age and of different curding time. It must be noted that there is a material variation in the curding time of the samples of cow's milk obtained from different sources and of different ages.

Since the effect of the modifier in delaying the curding time is a proportionate action there will necessarily be a less pronounced effect upon milk which has normally a short curding time than upon a sample of milk in which the normal curding time is longer. For instance, it will be observed that the normal curding time in the control in Table I is 4.5 minutes. The addition of the modifier in Experiment 1 delayed this to 13 minutes or 290%. In Table III the normal curding time of the control was 3.5 minutes. The addition of the modifying agents as used in Experiment 18, which were identical with those used in Experiment 1 prolonged the curding time to 6.6 minutes.

TABLE I.

Expt. No.	Formula modifier in grains. Lactose.	NaCl.	$NaHCO_3$.	$KHCO_3$.	Other.	Curd time.	Character of curd.	$\frac{\text{Time}}{\text{Control}}$.	Kind of milk.	
1	35	$^1/_6$	$^1/_2$	$^1/_{12}$	....	13	+	2.9	Whole	
2	26	$^1/_6$	$^1/_2$	$^1/_{12}$	$1^1/_2$ $CaCO_3$; $^1/_6$ Ca. L. Phos.	9.5	++	2.1	Whole	
3	..	..	..	..	....	4.5	+++	1.0	Whole	(Control)
4	35	$^1/_6$	$^1/_2$	$^1/_{12}$	....	13	+	2.9	Skim	
5	26	$^1/_6$	$^1/_2$	$^1/_{12}$	$1^1/_2$ $CaCO_3$; $^1/_6$ Ca. L. Phos.	10.7	++	2.4	Skim	
6	..	..	..	..	....	4.7	+++	1.0	Skim	(Control)
7	35	$^1/_6$	$^1/_2$	$^1/_{12}$	$1^1/_2$ $CaCO_3$	9.5	++	2.1	Whole	
8	35	$^1/_6$	$^1/_2$	$^1/_{12}$	$^1/_6$ Ca. L. Phos.	7.6	+++	1.7	Whole	
9	35	$^1/_6$	$^1/_2$	$^1/_{12}$	$1^1/_2$ $CaCO_3$; $^1/_6$ Ca. L. Phos.	9.0	++	2.0	Whole	
10	35	$^1/_6$	$^1/_2$	$^1/_{12}$	1 teasp. lime water	11.0	++	2.5	Whole	
11	35	$^1/_6$	$^1/_2$	$^1/_{12}$	$^1/_{10}$ $NaHPO_4$	14.0	+	3.1	Whole	
12	35	$^1/_6$	$^1/_2$	$^1/_{12}$	1 teasp. lime water; $^1/_{10}$ Na_2HPO_4	12.0	+	2.6	Whole	
13	..	..	..	..	1 gram maltose; 1 gram dextrin	6.7	+++	1.5	Whole	

Ca. L. Phos. = Calcium Lacto Phosphate.

$\frac{\text{Time}}{\text{Control}}$ = Ratio of delayed curding time to the normal curding time.

TABLE II.

Expt. No.	Formula modifier in grains. Lactose.	NaCl.	$NaHCO_3$.	$KHCO_3$.	Other.	Curd time.	Character of curd.	$\frac{\text{Time}}{\text{Control}}$.	Kind of milk.	
14	26	$^1/_6$	$^1/_2$	$^1/_{12}$	$^1/_2$ $CaCO_3$; $^1/_6$ Ca. L. Phos.	3.9	++	1.3	Whole	
15	35	$^1/_6$	$^1/_2$	$^1/_{12}$	....	5.4	+	1.8	Whole	
16	..	..	..	..	....	3.0	+++	1.0	Whole	(Control)

TABLE III.

17	26	$^1/_6$	$^1/_2$	$^1/_{12}$	$1^1/_2$ $CaCO_3$; $^1/_6$ Ca. L. Phos.	4.9	++	1.4	Whole	
18	35	$^1/_6$	$^1/_2$	$^1/_{12}$	....	6.6	+	1.9	Whole	
19	..	..	..	..	....	3.5	+++	1.0	Whole	(Control)

TABLE IV.

20	26	$^1/_6$	$^1/_2$	$^1/_{12}$	$1^1/_2$ $CaCO_3$; $^1/_6$ Ca. L. Phos.	4.8	++	1.4	Whole	
21	35	$^1/_6$	$^1/_2$	$^1/_{12}$	....	3.0	++	1.5	Whole	
22	35	$^1/_6$	$^1/_2$	$^1/_{12}$	$^1/_{10}$ Na_2HPO_4	3.2	+	1.6	Whole	
23	..	..	..	..	....	2.0	+++	1.0	Whole	(Control)

It will be observed that the addition of sodium phosphate as shown in Table I produced very satisfactory results both in delaying the time of curding and in changing the character of the curd. Bearing this fact in mind this agent was introduced in Experiment 22, as shown in Table IV. In this particular series of experiments the control showed a normal curding time of two minutes. In this case the addition of the modifying agent used in Experiment 1 delayed the curding time of this milk to 3 minutes, or 150%. The further addition of sodium phosphate, however, increased the curding time to 3.2 minutes, or 160%, showing the distinct gain by the addition of a small quantity of this agent.

CONCLUSIONS.

In all cases the toughness of the curd produced varies with the delay in curding which is caused by the modifying agent. Quick curding produces hard, tough clots while delayed curding forms a soft, fine mass. In a number of these experiments calcium carbonate and calcium lactophosphate were used, because practically all the milk modifiers on the market contain these ingredients. As indicated in our study of the theoretical considerations in a prëvious paragraph the fact was brought out that there were no adequate grounds for adding these constituents to agents intended to modify cow's milk and indeed their use is shown to be contra-indicated by these experiments.

A study of the results of these tables leads to the conclusion that the most satisfactory results in modification of cow's milk may be expected from the addition of the following ingredients: lactose, sodium chloride, sodium bicarbonate, potassium bicarbonate and sodium phosphate, omitting entirely the calcium salts which are commonly used in these modifying agents. We give below the proportions of these ingredients which from theoretical considerations and from laboratory experiments seemed best designed to meet the conditions ordinarily met with in modification of cow's milk for infant feeding.

FORMULA.

Lactose	35 grains
Sodium Chloride	$^1/_6$ grain
Sodium Bicarbonate	$^1/_2$ grain
Sodium Phosphate	$^1/_{10}$ grain
Potassium Bicarbonate	$^1/_{12}$ grain

This quantity of the different modifying agents should be added to four ounces of cow's milk, which should be diluted, of course, in accordance with the requirements of the individual infant.

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RESEARCH LABORATORY,
THE WM. S. MERRELL COMPANY,
CINCINNATI.

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