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LEUKOCYTE COUNTS DURING DIGESTION IN BOTTLE-FED INFANTS*

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It is the consensus of opinion, or belief of the majority of writers, that one of the physiologic causes of leukocytosis is digestion, or ingestion of food. It is the purpose of this paper to show that such is not constantly the case — at least in bottle-fed infants. Most of the text-books speak of physiologic leukocytosis. Some of the standard works on pediatrics state this leukocytosis to be more pronounced in children; a few speak of its being inconstant; and many ignore it entirely.

Yet it is very important whether this is, or is not, the case, especially in the interpretation of the leukocyte count in pathologic conditions.

REVIEW OF THE LITERATURE

The most striking thing in reviewing the literature on the subject is the fact that physiologic variations in leukocytes are seldom taken into account when drawing conclusions in a comparison of counts. Occasionally an attempt to avoid the disturbing factor of digestive leukocytosis in comparative counts is made,[1] for instance, by taking counts from three to five hours after a meal. The fallacy of this will become clear later on.

The first research in digestive leukocytosis was by Moleschott[2] in 1854. Following his work came that of Hirt[3] in 1856; Malassez[4] in 1876; Halla[5] in 1883; Reinecke[6] in 1883. These are all of interest historically, but as practical researches they do not stand because of poor methods of counting and small number of cases.

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1. Orr: Leukocyte and Differential Counts in Ward and Open Air Treatment, Am. Jour. Med. Sc., 1912, cxliv, p. 238.
2. Moleschott: Ueber das Verhaltnis der farblosen Blutkörperchen zu den farbigen in den verschiedenen Zuständen des Menschen, Wien. med. Wchnschr., 1854, No. 8, p. 113.
3. Hirt: Ueber das numerische Verhältnis zwischen den weissen und roten Blutkörperchen, Arch. f. Anat. u. Physiol., 1856, p. 174.
4. Malassez: Gaz. mêd. de Paris, 1876, No. 25, p. 297.
5. Halla: Ueber den Hämoglobingehalt des Blutes, etc., Ztschr. f. Heilk., 1883, iv, 198.
6. Reinecke: Ueber den Gehalt des Blutes an Körperchen, Virch. Arch. f. path. Anat., 1889, cxviii, 148.

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In 1892, Rieder[7] found that seventeen of twenty-five adults gave digestive leukocytosis, and eleven of twelve children; and that the children showed a higher or stronger leukocytosis than adults. He counted before, and only three hours after the midday meal, however, and counted few cells.

In 1892, Schwinge[8] carried out a small research on two adults and two children, examining the blood at two-hour intervals, and concluded that children showed more digestive leukocytosis than adults.

In 1898, Gregor,[9] in nine researches on healthy children, did not always find leukocytosis; very little in breast-fed children, and then only after many hours. In eight of fifteen babies with chronic injury of bowel function he found a distinct leukocytosis with protein supply. He concluded that it is not clear why one child has and another has not digestive leukocytosis; that in most cases after a hunger period protein food causes leukocytosis; that the maximum count is at the noon hours and after the chief meal.

In 1900, Japha[10] examined fourteen reasonably bowel healthy children of whom eight showed at some time after the meal a higher leukocytosis than before. Of these eight, three could be ruled out because of complications, or great irregularity in the counts, leaving only five of the fourteen. He concluded that one must not call every leukocytosis after a meal a digestive leukocytosis, as variations exist regardless of meals; that his work and that of others before him did not prove a digestive leukocytosis; that digestion and assimilation did not hang together; that as leukocytosis was not present under normal conditions one could not make any differential diagnosis in chronic dyspepsia and enteritis.

The same author[11] in 1901, in a few carefully made researches on his own person, came to the conclusion that adults showed a digestive leukocytosis in a limited sense, in that it occurred after the noon meal, at which time there was a periodical increase of the white blood cells regardless of food. He further stated that the rise was not constant and was hindered by constipation. The increase was mostly in the polymorphonuclear cells.

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7. Rieder: Beitrag zur Kenntnis der Leukocytosis und verwandter Züstände des Blutes, Leipsic, 1892, F. C. W. Vogel.

8. Schwinge: Ueber den Hämoglobingehalt, etc., Arch. f. d. ges. Physiol., 1898, lxxiii, 299.

9. Gregor: Untersuchungen über Verdauungs-Leukocytose bei magendarmkranken Säuglingen, Arch. f. Verdauungskrankh., 1898, iii, 387.

10. Japha: Die Leukocyten beim gesunden und kranken Säugling, Jahrb. f. Kinderh., 1900, p. 242.

11. Japha: Ueber Verdauungs-Leukocytose, Deutsch. Aerzt., Zeitung, 1901, iii, 145.

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In 1904 Moro[12] examined seven children. He found that digestive leukocytosis was inconstant, although it did occur on the first cow's milk meal to a breast-fed baby, and he considered this a reaction against foreign protein.

In 1911 Wernstedt[13] examined about twenty-seven children. He found that the curves of leukocytes resembled irregular fever curves regardless of whether the infant was fed breast milk, boiled breast milk, cow's milk, or whether it was the first meal of a new-born baby. His charts show that the average of counts after meals were seldom higher than before. He believed that rest or motion, sleep or wakefulness had considerable influence on the count, and his highest counts were on crying children and the lowest on those in sleep or rest.

There have been many researches to determine the cause of digestive leukocytosis.

Hofmeister[14] found that in the intestine of a cat under the influence of food the lymph cells rose in number and that the lymph vessels filled. This was chiefly in the stomach and upper small intestine. Heidenhain,[15] however, thought that in the thoracic duct the cells were too few and the chyle protein too small in amount to account for the supply in the body.

Pohl,[16] in fifty trials on a dog, always obtained digestive leukocytosis (with three exceptions) when protein food was given. He claimed from his examinations that the intestinal veins were richer in white blood cells than the arteries, and believed this to be the source of the cellular increase after the ingestion of food.

Rieder[7] could not demonstrate this, and thinks the increase is due to a chemotaxis phenomenon, the digestive products in the blood causing an attraction.

Muller[17] found that a prolonged hunger period followed by a protein rich meal gave leukocytosis. Burian and Schur[18] also found that an eighteen-hour hunger period followed by a protein meal caused

12. Moro: Vergleichende Studien über die Verdauungsleukocytose beim Säugling, Arch. f. Kinderh., 1904, xl, 39.

13. Wernstedt: Bidrag till fragen förekomsten af en digestion Leukocytos, etc., Nord. med. Ark., Stockholm, 1910, 3, f, afd. ii, No. 6, p. 1.

14. Hofmeister: Ueber Resorption und Assimilation der Nährstoffe, Arch. f. exper. path. u. Pharmakol., 1886-7, xxii, 306.

15. Heidenhain: Beiträge zur Histologie und Physiologie der Dünndarmschleimhaut, Arch. f. d. ges. Physiol., 1888, xliii, supplement, p. 1.

16. Pohl: Ueber Resorption und Assimilation der Nährstoffe; Die Vermehrung der farblosen Zellen im Blute nach Nahrungsaufnahme, Arch. f. exper. Path. u. Pharmakol., 1889, xxv, 31.

17. Müller: Klinische Beobachtungen über Verdauungs-Leukocytose, Prag. med. Wchnschr., 1890, xv, 213, 228, 239.

18. Burian und Schur: Verdauungsleukocytose und Verdauung, Wien. klin. Wchnschr., 1897, x, 137.

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leukocytosis. They could find no relation to nitrogen excretion, and believed the phenomenon not to be one of resorption, but a reaction against injurious foodstuffs.

The results of von Limbeck[19] were similar to those of Burian and Schur, and he also thought constipation hindered the result.

Reinert[20] from his examinations came to the conclusion that the lowest count of the day was in the morning (six to ten), and the highest about four in the afternoon. He thought food made very little difference.

Goodall, Gulland and Paton[21] in 1903, and Goodall and Paton[22] in 1905 did considerable work on dogs and cats. During the course of digestion they simultaneously examined the blood from the mesenteric veins and arteries, and the bone marrow. Their conclusions were that leukocytosis was present after meals, its maximum being at about four hours; that it was both a polymorphonuclear and a lymphatic increase; that the number and variety of cells were the same in the mesenteric arteries and veins, but much increased in the blood from the bone marrow; and they considered this to be the source of the increased number of cells in the blood during digestion. Removal of the spleen did not hinder the production of leukocytosis.

Finkelstein[23] believed it was the whey content and not the protein which determined the production of leukocytosis during digestion. So also Rosenstern,[24] who believed the rise in cells was a reaction analogous to the fever reaction in ingestion of sugar and salts. He examined only ten children, and made his counts only about three to five times a day.

It is interesting to note that Argand and Billard[25] found in examining two rabbits that starvation caused a leukopenia with mononuclear cells predominating which quickly returned to normal on feeding.

19. Von Limbeck: Klinisches und Experimentelles über die Entzündliche Leukocytose, Ztschr. f. Heilk., 1889, x, 392.

20. Reinert: Die Zählung der Blutkörperchen und ihre Bedeutung fur die Diagnose und Therapie, Leipsic, 1891, F. C. W. Vogel.

21. Goodall, Gulland and Paton: Digestive Leucocytosis in Normal and in Spleenless Dogs, Jour. Physiol., London, 1903, xxx, 1.

22. Goodall and Paton: Digestion Leucocytosis, Source of the Leucocytes, Jour. Physiol., London, 1905, xxxiii, 20.

23. Finkelstein: Verhandlungen der Gesellschaft für Kinderheilkunde, 1906, xxiii, 160.

24. Rosenstern: Ueber alimentäre Leukocytose, Monatschr. f. Kinderh., Leipsic, 1909, viii, 9.

25. Argand and Billiard: Inversion de la formule leucocytaire sous l'influence de l'inanition, Compt. rend. Soc. de Biol., Paris, 1911, lxx, 146.

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Richet,[26] in working on a dog, found that uncooked albuminoid matter produced leukocytosis, and cooked did not, even in enormous doses. He concluded that the reaction was due to certain albuminoid substances escaping the action of the digestive juices and entering the blood.

This review of the literature contains most of the original work done on the subject. It does not contain all, as some of the articles were not accessible. It is enough, however, to give us the ideas of the majority of authors and researchers, which may be summarized as follows:

1. In babies digestive leukocytosis is inconstant.
2. In adults digestive leukocytosis is inconstant.
3. A rise occurs in the early afternoon regardless of food.
4. Animals such as dogs, cats and rabbits do show a leukocytosis after food high in protein.
5. The majority of researchers think protein food to be necessary for the production, and a few think the whey and sugar content to be the cause.

It is significant that much of the work has been done on animals.

OBSERVATIONS ON FIFTY CHILDREN

The present report consists of a study of fifty children, on whom over seven hundred blood counts were made.

The method of study pursued was to take a leukocyte count immediately before feeding, immediately after feeding, fifteen minutes after feeding, one-half hour after, one hour after, one and a half hours after, and so on every half-hour until the next feeding. These groups of blood counts (beginning before one feeding, and ending before another) are taken to constitute a "series" and will be spoken of as such. There are 120 of these "series" in this report.

The leukocytes were counted with the low power; four smears were made on the Jappert-Ewing counting chamber; and the contents of two large squares counted on each, making a total of eight large squares.

All matters of technic were carefully watched, and the same pipette and counting chamber used during a series. The toes were found to be the most convenient part of the anatomy for the removal of blood. As far as possible the same amount of pressure was used in extracting blood, and all causes of local congestion avoided. For example, instead of using one toe during a series, different toes were used.

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26. Richet: La réaction leucocytaire: digestion, etc. Presse. méd., 1913, xxi, 539.

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The infants on whom this study was made were all bottle-fed, and, while not exactly normal children, were of the type usually seen in a hospital ready for discharge. They were practically all somewhat underweight for their age. With one or two exceptions they could be classed under three groups: "Convalescent Pneumonia," "Convalescent Gastro-Enteritis" and "Feeding." Eight of these babies were examined during one feeding period only, but all the rest had two or more series made, some running as high as twelve or thirteen.

The results of the analysis of these cases are interesting, in that physiological leukocytosis after feeding was not found in most instances, and the opposite condition of leukopenia prevailed. A single rise in leukocytosis after a meal was not considered a digestive increase unless it persisted, as it may be due to other causes. As pointed out by Wernstedt,[13] it may be the result of crying or great muscular activity. Also in judging of the increase or decrease, the mean of the counts after the meal (that is, during the series) was compared to the count before the meal. As examples of what the extraneous sources of increased leukocyte count may be, see illustrative cases — 6, 7, 8 and 9. These cases show that striking a small artery, crying, cold extremities necessitating much pressure to extract the blood, and getting the blood from a place previously punctured, may be the causes of increased leukocyte counts. When such factors as these could be determined, the increase in leukocyte count was not taken to be a digestive one. The frequency with which such things occurred may be judged by the fact that if these were not carefully ruled out, seventy-five of the 120 series would show an increased count during the digestive period, instead of the forty-four (or 28.3 per cent.) shown below.

Of the fifty children, only six, or 12 per cent., constantly showed an increase in the white blood cells during digestion, although sixteen, or 32 per cent., showed at times an increase, and at others a decrease. Contrasted with this, twenty-eight, or 56 per cent., constantly showed a decrease in leukocytes during digestion.

In considering the 120 series, 28.3 per cent. showed leukocytosis and 68.3 per cent. leukopenia. The remaining 3.3 per cent. were so irregular as to be undeterminable.

A study of Charts 1 and 2 will show the amount of leukopenia and when it occurs. The charts represent a summary of the fourth- and third-hour cases, respectively.

The curves, while irregular, clearly show the drop which in fourth-hour cases is greatest at one hour and reaches over 9 per cent., and in the third-hour cases is greatest between one and a half to two and a half hours, and reaches over 11 per cent.

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SUMMARY OF CASES

No.	Diagnosis	Age in Months	Gaining + Losing —	Stools During Day	Food	Average Count of Series	Time of Count	After Food, Leukocytosis + Leukopenia —
1	Slight enteritis ..... Underweight.	8	+	Three to six greenish-yellow, soft; few curds.	Casein milk, 3.7-1.6-3, 4 oz.	14,325	9-12 a. m.	—
					Casein milk, 3.7-1.6-3, 4 oz.	17,020	9-12 p. m.	—
2	Normal except for slight anemia.	14	—	One formed yellow.....	4-4.5-3.5. Whole milk, 8 oz.	13,700	9-12 a. m.	+
					4-4.5-3.5. Whole milk, 8 oz.	13,400	9-12 p. m.	+
3	Normal convalescent gastro-enteritis.	8	+	Two soft yellow.....	2.6-3-2.3, 7½ oz.	12,025	?	+
					2.6-3-2.3; 7½ oz.	11,960	?	+
4	Normal convalescent slight gastro-enteritis.	10	+	Two soft yellow, with few curds.	⅔ milk, 4 oz.	15,500	9-12 a. m.	—
				Two soft yellow, with few curds.	⅔ milk, 4 oz.	12,990	9-12 a. m.	—
				Two soft yellow, with few curds.	⅔ milk, 4 oz.	13,725	1- 4 p. m.	—
5	Feeding ..... Later developed pertussis.	4	Stationary	Three soft yellow.....	2-6-2, 3 oz.	15,090	9-12 p. m.	+
					3-6-2, 4 oz.	21,450	3- 6 p. m.	—
6	Normal convalescent gastro-enteritis..	4	+	Soft yellow	⅔ milk and 3% sugar, 5½ oz.	14,160	9-12 p. m.	+
				Constipated, greenish-yellow.	3-6-2.5, 5½ oz.	18,420	9-12 a. m.	—
7	Feeding ..... Convalescent from sugar injury.	7	+	One soft yellow.....	Casein milk with cream, 5 oz., 3.6-1.7-3.04	13,700	9-12 a. m.	—
				One soft yellow.....	Casein milk with cream, 5½ oz., 3.6-1.7-3.04	15,110	12- 3 p. m.	+
8	Feeding	½ to 1½	Stationary	Two greenish-yellow, with fine curds.	2.5-4-1.5, 2 oz.	14,990	11- 1 a. m.	—
			Stationary	Two greenish-yellow, with fine curds.	Whey, cream, 1.3-5.2-1.2	18,160	11- 1 a. m.	—
			Stationary	Three greenish-yellow with fine curds.	Whey, cream, 1.7-5-1.2, 2½ oz.	14,880	11- 1 a. m.	—
			+	Four soft brown.....	2-7-2, 3½ oz. malt soup	15,050	11:30 a. m.-2 p. m.	—
			+	Four soft brown.....	2-7-2, 3½ oz. malt soup	15,040	2-4:30 p. m.	—
9	Feeding	3	Stationary	One loose greenish--yellow, with fine curds.	½ milk and 2% dextro maltose, 4 oz.	15,290	9-12 a. m.	+
			Stationary	One loose greenish--yellow, with fine curds.	½ milk and 2% dextro maltose, 4 oz.	14,570	12- 3 p. m.	+
10	Normal convalescent from gastro-enteritis.	8½	+	Three soft yellow.....	3-6-3, 7½ oz.	18,250	9-12 a. m.	—

11	Normal	20	Stationary	One formed yellow.....	Whole milk, 8 oz.	9,660	?	—
			Stationary	One formed yellow.....	Whole milk, 8 oz.	13,750	?	—
12	Normal convalescent from gastro-intestinal indigestion	8½	+	Four soft yellow.....	4.5-4.4-2.57, 7 oz., whey, cream.	12,470	9- 1 a. m.	—
			+	Four soft yellow.....	3-6.5-2.7, 7 oz., milk mixt.	11,500	1- 5 p. m.	—
13	Normal convalescent pneumonia. Developed pertussis.	24	—	0	Whole milk, 8 oz.	8,570	9-12 p. m.	—
			Stationary	0	Whole milk, 8 oz.	10,620	9- 1 a. m.	? (vacillation)
			Stationary	0	Cream wheat, 1 saucerful	10,660	3 p. m.	—
			Stationary	0	Junket, 1 saucerful.....	9,720	7 p. m.	—
			Stationary	0	Whole milk, 2 oz.	8,800	9 p. m.	—
			Stationary	One soft yellow.....	Whole milk, 8 oz., plus cream wheat.	9,080	9- 1 a. m.	+
			Stationary	One soft yellow.....	Whole milk, 8 oz., plus toast.	8,150	1- 5 p. m.	+
			+	One soft yellow.....	Whole milk, 5 oz., cream wheat.	15,030	1- 5 p. m.	? (vacillation)
			+	One soft yellow.....	Whole milk, 8 oz.	13,920	5- 9 p. m.	—
			+	One soft yellow.....	Whole milk, 8 oz.	15,140	9-12 p. m.	+
			Stationary	0	Oatmeal, 1 saucerful.....	18,530	9- 1 a. m.	+
			Stationary	0	Whole milk, 8 oz.	16,380	9-12 p. m.	—
			+	One loose greenish-yellow	Whole milk, 8 oz.	18,400	1- 5 p. m.	+
14	Normal convalescent pneumonia.	24	Stationary	One hard yellow.....	¾ milk, 8 oz.	12,500	1- 5 p. m.	—
			+	One soft yellow.....	Whole milk, 7 oz.	18,200	9- 1 a. m.	+
			+	One soft yellow.....	Whole milk, 8 oz.	15,500	9-12 p. m.	—
			Stationary	One loose greenish-yellow, with fine curds.	Whole milk, 8 oz., and cream wheat.	16,350	9- 1 a. m.	—
15	Otitis media ..... Gastro-intestinal tract O.K.	30	Stationary	Two soft brown.....	Whole milk, 8 oz.	19,300	5- 9 p. m.	—
			Stationary	Two soft brown.....	Whole milk, 8 oz.	18,980	9-12 p. m.	—
16	Convalescent pneumonia	15	Stationary	Two pasty yellow.....	Whole milk, 8 oz.	18,640	1- 5 p. m.	—
			+	Two soft greenish-yellow	Whole milk, 8 oz.	17,780	1- 5 p. m.	+
			+	Two soft greenish-yellow	Whole milk, 8 oz.	18,650	9- 1 a. m.	+
17	Gastro-intestinal indigestion Sugar in urine vomiting. Later cleaned up.	7	—	Three soft yellow.....	3-5.3-2.6, 3 oz., whey, cream.	18,930	9-12 p m	—
			—	Two soft yellow, with fine curds.	0.58-5-1.9, 8 oz., whey, skimmed milk.	18,500	9- 1 a. m.	—
			—	Two soft yellow, with fine curds.	0.58-5-1.9, 8 oz., whey, skimmed milk.	18,110	1- 5 p. m.	+
			—	Two soft yellow, with fine curds.	0.58-5-1.9, 8 oz., whey, skimmed milk.	17,390	5- 9 p. m.	—
			—	Two soft yellow, with fine curds.	0.58-5-1.9, 8 oz., whey, skimmed milk.	18,730	9-12 p. m.	+
18	Feeding, premature.....	3½	Stationary	Two soft yellow.....	2-7-2, 3½ oz. malt soup	8,850	1- 5 p. m.	—
			Stationary	Two soft yellow.....	2-7-2, 3½ oz. malt soup	12,450	5- 9 p. m.	—
			Stationary	Two soft yellow.....	2-7-2, 3½ oz. malt soup	9,540	9-12 p. m.	—

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SUMMARY OF CASES—Continued

No.	Diagnosis	Age in Months	Gaining + Losing —	Stools During Day	Food	Average Count of Series	Time of Count	After Food, Leukocytosis + Leukopenia —
19	Feeding	8	+	Three pasty yellow, with fine curds.	3.5-5-3.5, 7 oz.	10,870	9-12 p. m.	—
			+	Three pasty yellow, with fine curds.	3.5-5-3.5, 7 oz.	9,880	12- 3 p. m.	—
			+	One pasty yellow	3.5-5-3.5, 7 oz.	11,800	1- 5 p. m.	—
20	Bronchitis Gastro-intestinal tract normal.	22	+	One constipated yellow...	Oatmeal and whole milk, 5 oz.	20,200	9- 1 a. m.	? (vacillation)
			+	One constipated yellow...	Egg and toast and whole milk, 8 oz.	18,250	1- 5 p. m.	—
			+	One constipated yellow...	Junket, whole milk, 3 oz.	22,490	5- 9 p. m.	? (vacillation)
21	Gastro-intestinal indigestion	15	+	Four soft greenish-yellow, with fine curds.	2.7-3.1-2.5, 8½ oz., milk and soy bean.	15,400	1- 5 p. m.	—
			+	Three soft yellow	2.7-3.1-2.5, 8½ oz., milk and soy bean.	12,700	9- 1 a. m.	—
			+	Three soft yellow	2.7-3.1-2.5, 8½ oz., milk and soy bean.	13,860	1- 5 p. m.	+
			+	One soft yellow, with flie curds.	3.13-3.9-2.8, 8 oz., milk, soy bean.	14,540	9- 1 a. m.	+
			+	One soft yellow, with flie curds.	3.13-3.9-2.8, 8 oz., milk, soy bean.	14,230	1- 5 p. m.	+
			Stationary	One pasty dark green....	2.5-1.5-2, 6 oz., casein milk	16,300	1- 5 p. m.	—
			Stationary	One pasty dark green....	2.5-1.5-2, 6 oz., casein milk	17,120	9-12 p. m.	—
			+	One soft brown, with fine curds.	2-7-2, malt soup	23,940	9-12 p. m.	—
22	Feeding, tuberculosis (?)	19	+	One soft yellow	Whole milk, 6 oz.	11,400	?	—
23	Normal convalescent gastro-enteritis.	5	Stationary	Two soft yellow	⅔ milk and 3% dextro maltose, 5 oz.	16,630	9-12 a. m.	—
24	Feeding	8	Stationary	Two soft yellow, with casein curds.	2.5-5-2.5, 6 oz.	10,160	9-12 a. m.	—
			Stationary	Two soft yellow, with casein curds.	2.5-5-2.5, 6 oz.	9,880	12- 3 p. m.	—
25	Feeding	5	Stationary	Two loose brown, with mucus.	Water, 5 oz.	7,960	9-12 a. m.	—
			Stationary	Two loose greenish-yellow	No food	9,950	9-12 a. m.	—
26	Feeding	7½	Stationary	Three pasty yellow, with fine curds.	⅔ milk, 6 oz.	12,310	9-12 a. m.	+
			Stationary	Three pasty yellow, with fine curds.	⅔ milk, 6 oz.	12,720	12- 3 p. m.	—

27	Convalescent enteritis	5	—	Two soft greenish-yellow, with some mucus.	⅔ milk and 2% dextro maltose, 4 oz.	11,600	9-12 a. m.	—
			—	Two soft greenish-yellow, with some mucus.	⅔ milk and 2% dextro maltose, 4½ oz.	11,390	12- 3 p. m.	—
		5½	+	Three soft yellow.....	⅔ milk and 2% sugar, 4½ oz.	17,150	9-12 a. m.	—
28	Feeding	3	Stationary	Three spongy yellow.....	½ milk and 3% dextro maltose, 3½ oz.	10,690	9-12 a. m.	—
29	Feeding	5½	—	Three soft yellow, with fine curds.	⅔ milk and 3% dextro maltose, 5 oz.	5,940	9-12 a. m.	+
			—	Three soft yellow, with fine curds.	⅔ milk and 3% dextro maltose, 5 oz.	5,760	12- 3 p. m.	—
30	Feeding	4½	—	One soft yellow, with fine curds.	2.5-1.4-3, 5½ oz., cosein milk.	91,300	9-12 a. m.	+
			+	Two soft yellow.....	2.5-1.4-3, 6½ oz., casein milk.	13,140	9-12 a. m.	+
31	Feeding ..... Slight intoxication?	8	— !!	Three loose yellow, with fine and casein curds.	¾ milk, 6 oz., boiled....	14,980	1- 5 p. m.	++
			—	Four loose greenish-yellow, with fine curds.	2-5-2, 4 oz.	31,470	9-12 a. m.	— No apparent cause for high count.
32	Slight gastro-enteritis	7½	+	Two loose greenish, with mucus.	½ milk and 3% dextro maltose, 5 oz.	8,830	9-12 a. m.	—
33	Feeding ..... Ulceration mouth.	6	—	Two loose yellow	Buttermilk, 5 oz.	11,800	9-12 a. m.	+
			—	Two soft yellow	Buttermilk, 5 oz.	13,980	9-12 a. m.	—
34	Convalescent gastro-enteritis	14	+	Two loose yellow.....	2.5-3.5-3, casein milk and dextro maltose, 5½ oz.	6,390	9-12 a. m.	—
				Two loose yellow.....	2.5-3.5-3, casein milk and dextro maltose, 5½ oz.	6,920	12- 3 p. m.	—
35	Feeding	15½	+	One constipated yellow..	⅔ milk, 5 oz.	13,400	9- 1 a. m.	—
36	Convalescent gastro-enteritis	7½	+	Two soft yellow.....	½ milk and soy bean, 6 oz.	8,810	9- 1 a. m.	—
				Two soft yellow.....	½ milk and soy bean, 6 oz.	8,070	1- 5 p. m.	+
37	Convalescent gastro-enteritis	8	Stationary	One loose greenish-yellow	2-6-3, 8 oz.	23,800	9- 1 a. m.	+ No apparent reason for high count.
			Stationary	One loose greenish-yellow	2-6-3, 8 oz.	20,580	1- 5 p. m.	+
38	Convalescent gastro-enteritis	7	Stationary	Two soft whitish, with fine curds.	⅔ milk, 6 oz.	11,450	1- 5 p. m.	+
			+	Three soft whitish, with fine curds.	⅔ milk 5½ oz.	9,100	1- 5 p. m.	—

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SUMMARY OF CASES—Continued

No.	Diagnosis	Age in Months	Gaining + Losing —	Stools During Day	Food	Average Count of Series	Time of Count	After Food, Leukocytosis + Leukopenia —
39	Convalescent gastro-enteritis Slight bronchitis.	6	—	Two soft greenish-yellow, with fine curds.	2.5-4-2.2, 2 oz.	14,790	9- 1 a. m.	—
			—	Two soft greenish-yellow, with fine curds.	2.5-4-2.2, 2 oz.	16,400	1- 5 p. m.	+
40	Normal	15½	+	Two pasty yellow	Whole milk, 8 oz.	10,220	9- 1 a. m.	+
41	Normal	26	?	?	Whole milk, 8 oz.	10,080	1- 5 p. m.	—
42	Feeding	17	+	One loose yellow	¾ milk, 5 oz.	10,870	1- 5 p. m.	—
			+	One soft yellow	¾ milk, 5 oz.	10,680	1- 5 p. m.	—
43	Feeding	11½	Stationary	Three pasty greenish-yellow.	Buttermilk, 4 oz.	5,870	9- 1 a. m.	—
44	Feeding Convalescent essential edema.	19½	+	Two constipated yellow..	Whole milk, 7½ oz.	8,070	9- 1 a. m.	—
45	Feeding	7½	Stationary	Two loose greenish-yellow, with casein curds.	½ milk and soy bean	16,890	9- 1 a. m.	—
			Stationary	Three constipated yellow	No food	16,850	1- 5 p. m.	—
46	Convalescent enteritis	11	Stationary	Two soft yellow	¾ milk and 2% dextro maltose, 8 oz.	9,840	9- 1 a. m.	—
47	Feeding	3	+	Soft yellow	No food	15,260	9-12 a. m.	—
			Stationary	Soft yellow	?, i. e., food unknown...	14,400	9-12 a. m.	—
48	Feeding Convalescent gastro-enteritis.	9½	+	Three soft yellow	¾ milk, 7 oz.	14,920	9- 1 a. m.	—
			+	Three soft yellow	¾ milk, 7 oz.	13,930	1- 5 p. m.	—
49	Feeding Bronchitis.	5	Stationary	Three loose greenish-yellow.	⅔ milk, 4 oz.	12,640	9-12 a. m.	—
			Stationary	Three loose greenish-yellow.	⅔ milk, 4 oz.	12,760	9-12 a. m.	—
50	Normal convalescent enteritis.	7	Stationary	Two soft yellow, with fine curds.	2.5-4-2, 7 oz.	12,430	9- 1 a. m.	—
			Stationary	Two soft yellow, with fine curds.	2.5-4-2, 7 oz.	10,270	1- 5 p. m.	—
			+	Two soft yellow	No food	9,260	9- 1 a. m.	—

The explanation of the fall after the third hour in Chart 1 lies in the fact that this curve, being a composite one of all fourth-hour cases, represents series taken at different times of the day. If we take into consideration the fact that the highest count of the day is before the morning feeding, we have a ready explanation of this peculiar fall.

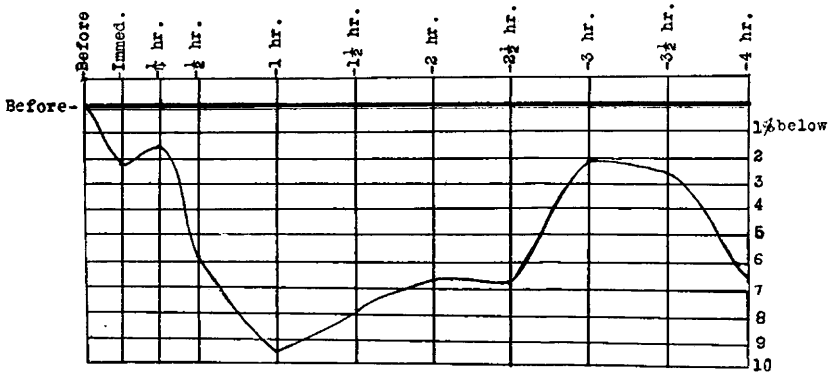

Chart 1.—Fourth-hour cases. In this and the following chart the vertical lines represent time and the horizontal percentages.

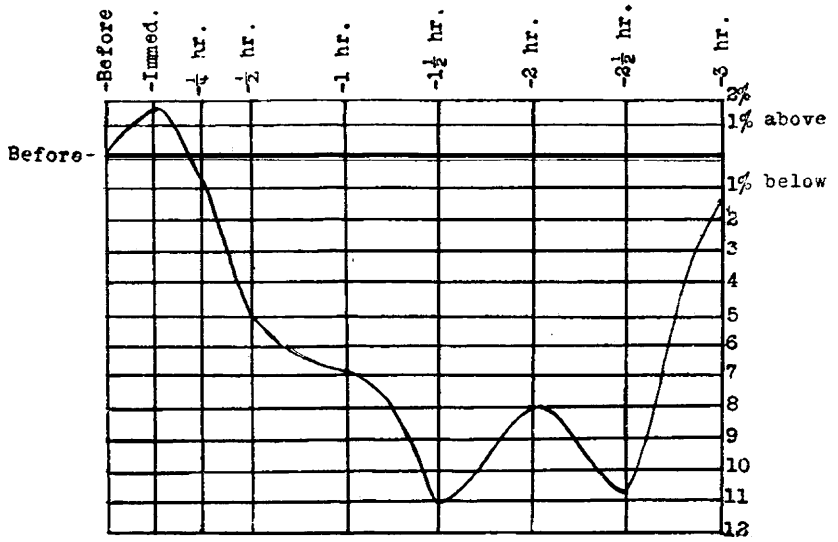

Chart 2.—Third-hour cases.

As this is not marked until about four or five hours after the first morning feeding, it affects the third-hour cases but little. This does not correspond to the findings of Gregor,[9] Japha[11] and others. Of twenty-two cases in the present report which were studied both in morning and afternoon, however, ten showed a higher average of

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counts in the morning, eight showed about the same both morning and afternoon, and only four showed a higher average of counts in the afternoon.

Age.—The patients varied from 3 weeks to 26 months in age. No relation of digestive leukocytosis or leukopenia could be established according to age grouping.

Nature of Food.—The majority of the patients were fed on cow's milk mixtures, although a few had casein milk, malt soup, whey and cream, and buttermilk mixtures. The number of patients fed on other than cow's milk mixtures was too small to permit judgment of their relation to leukocytosis or leukopenia.

Temperature.—No relation between leukocytosis and leukopenia, and temperature could be established.

Gain or Loss in Weight.—Of the 120 series at the time of counting, fifty-six, or 46.66 per cent., were gaining in weight; nineteen, or 15.83 per cent., were losing, and forty-five, or 37.5 per cent., were stationary in weight. The proportions of these three groups showing digestive leukocytosis or leukopenia may be shown in the following tabulation:

	Leukocytosis Per Cent.	Leukopenia Per Cent.	No Change or Vacillation Obscured Per Cent.
Gaining (56 series).....	26.78	66.07	7.14
Losing (19 series)	47.36	52.63	0
Stationary (45 series)	22.22	75.55	2.22

Briefly, then, these percentages show that leukocytosis during digestion occurred about twice as frequently in children losing weight as in those gaining or stationary, and that leukopenia is somewhat more constant in children gaining or stationary than in those losing weight.

Time of Day.—The relation to the time of day is shown in the following tabulation:

	Leukocytosis Per Cent.	Leukopenia Per Cent.	No Change Per Cent.
Morning or first feeding (51 series)	27.45	68.62	3.92
Early afternoon or second feeding (39 series)	33.33	64.1	2.56
Late afternoon or third feeding (8 series)	(All showed leukopenia)		
Last feeding or 9 p. m. feeding (18 series)	27.7	66.6	5.5

There does not, therefore, seem to be much relation to the time of day, unless we consider the small number of series taken during the late afternoon feeding.

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ILLUSTRATIVE CASES

The counts do not show a regular progressive decrease or increase as the case may be, but are often quite changeable and variable.

For example:

CASE 1.—Showing counts taken during four-hour period, the child receiving no food for several hours before or during the series.

At 9 a. m., white blood cells, 11,000; 9:30 a. m., 10,150; 10 a. m., 9,300; 10:30 a. m., 7,925; 11 a. m., 10,575; 11:30 a. m., 8,540; 12 noon, 7,725; 1 p. m., 8,900. This same child had shown on two other occasions a leukopenia following ingestion of food.

CASE 2.—A child convalescent from acute gastro-enteritis. He is now 13 months old, having normal temperature, and one or two firm, yellow bowel movements a day. Showing leukopenia.

At 9 a. m., white blood cells were 8,475; at 9:02 he was given 5½ ounces of casein milk with 2 per cent. sugar added (2.5-3.5-3); he finished his bottle at 9:15, and blood taken at that time showed a count of 5,875; a quarter of an hour later, white blood cells 6,825; half an hour later, 5,350; one hour, 4,900; one and one-half hours, 6,225; two hours, 5,475; two and one-half hours, 7,125; three hours, 7,275.

CASE 3.—The patient is a child of 1 year, convalescent from an acute gastro-intestinal upset. He is now gaining and having good stools.

At 9:20 a. m., his leukocytes were 6,600; at 9:24, he was given a buttermilk mixture of which he took 4 ounces, and finished this at 9:32. At that time his leukocytes were 5,800; a quarter of an hour later they were 5,700; half an hour, 6,150; one hour, 5,600; one and a half hours, 5,000; two hours, 5,950; two and one-half hours, 5,800; three hours, 6,800; three and three-fourth hours, 5,250.

CASE 4.—A child of 20 months, whose diagnosis was essential edema, but who at the present time is an entirely normal child.

Before his feeding of 7½ ounces of whole milk, his leukocytes were 9,550; half an hour after finishing this bottle, they were 8,600; one hour, 6,600; one and a half hours, 7,360; two hours, 6,300; two and one-half hours, 8,060; three hours, 7,960; three and three-fourth hours, 10,130.

CASE 5.—A child of 8 months, who is not doing very well at the time of examination, as she is having loose, greenish-yellow bowel movements and is vomiting somewhat. She shows a distinct leukocytosis after food.

Before food her count was 18,625. She was fed 8 ounces of a 2-6-3 milk mixture, and immediately regurgitated a small amount. A quarter hour after food her white blood cells were 32,050; half an hour, 28,350; one hour, 25,500; one and a half hours, 24,300; two hours, 23,650; two and one-half hours, 25,800; three hours, 21,850; three and one-half hours, 19,200; four hours, 18,700.

CASE 6.—Showing effect of cold. Before food, 16,675. Fed 6 ounces milk, 3 ounces soy bean gruel. One-half hour afterward, 13,825; one and one-half hours, 17,325 (toes very cold from exposure); two hours, 13,875 (toes warm again); three and one-half hours, 15,275.

CASE 7.—Showing the effect of removing blood from a puncture made some time previously. Before food, 10,425. Fed 6 ounces milk, 2 ounces soy bean gruel. Quarter hour afterward, 13,850; half an hour, 14,675; one hour, 14,400; two hours, 20,950 (blood removed from puncture made at one hour previously), three hours, 12,950.

CASE 8.—Showing the effect of crying. Before food, 10,250. Fed 8 ounces whole milk and two crackers; a quarter of an hour afterward, 9,125; half an hour, 12,000 (crying and struggling); one hour, 10,350; one and a half hours, 7,865; two hours, 9,525; two and one-half hours, 9,415; three hours, 10,600; three and one-half hours, 11,275; four hours, 10,475.

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CASE 9.—Showing the effect of arterial bleeding. Before, 11,050. Fed 3-5-3 mixture, 8 ounces; a quarter of an hour afterward, 10,000; half an hour, 9,750; one hour, 10,500; one and a half hours, 12,300 (struck small artery in big toe); two hours, 8,800; two and one-half hours, 8,050; three hours, 8,250; three hours and fifty minutes, 8,700.

CASE 10.—Child showing distinct leukocytosis after ingestion of food. Before, 9,800. Fed ⅔ milk, 6 ounces. Immediately after taking, 9,250; a quarter of an hour afterward, 11,600; half an hour, 10,500; three quarters of an hour, 12,300; one hour, 12,600; one and a half hours, 11,450; two hours, 12,100; two and one-half hours, 11,550; three hours, 11,600; three and one-half hours, 14,200; three and three-fourths hours, 9,900.

CASE 11.—Showing a child followed directly through morning and afternoon feedings, and having a slight but not continued rise after the second meal of the day. Before first morning feeding, 9 a. m., white blood cells, 12,700. Fed 3 ounces milk and 3 ounces soy bean gruel. Quarter hour afterward, 7,625; half an hour, 9,925; one hour, 7,100; one and a half hours, 8,600; two hours, 9,050; two and one-half hours, 7,975; three hours, 8,275; four hours, 8,050. Then fed 3 ounces milk and 3 ounces soy bean gruel. Immediately afterward the white blood cells were 9,025; half an hour afterward, 8,275; one hour, 7,500; two hours, 7,625; two and one-half hours, 7,925; three hours, 7,400; three and one-half hours, 7,350; four hours, 9,500.

A summary of the actual counts on uncomplicated cases shows the following figures for different ages:

Age	Average	Minimum	Maximum	No. Counts
1- 4 months	13,870	8,850	15,290	78
4- 8 months	12,360	7,960	17,150	254
8-12 months	12,290	9,880	15,500	115
12-18 months	12,820	6,390	17,120	103
18-24 months	10,720	8,070	13,750	21
Over 24 months.....	11,520	8,150	16,350	62

Remember these counts are on bottle-fed babies. Carstanjen,[27] in a number of counts, claims the average to be 12,500 in the first year. Rabinowitsch[28] thinks the counts usually given are too high, and says that healthy children from 1 to 16 years should average from 6,000 to 7,000.

CAUSE

As to why some children show leukocytosis and others leukopenia after food, and why the same child may show at times an increase and at times a decrease after food — this research offers no adequate explanation. Careful study of the cases as regards age, gain or loss in weight, character of stools, nature of food, temperature, and time of day did not show any definite relation. It might be added in this connection that six children were studied through a four-hour period,

27. Carstanjen: Wie verhalten sich die procentischen Vehrhältnisse der verschiedenen Formen der weissen Blutkörperchen beim Menschen unter normalen Umständen? Jahrb. f. Kinderh., 1900, lii, 333.

28. Rabinowitsch: Die Leukocyten verschiedenen Altersstufen: Untersuchungen über die Leucocyten gesunder Kinder, Arch. f. Kinderh., 1912, lix, 161.

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beginning at 9 a. m., and received no food then or for several hours before. These all showed a gradually decreasing leukocyte count.

A theory which may be offered here is that ingestion of food, and beginning of the activities of the gastro-intestinal tract, both glandular secretion and muscular movement thus causing increased blood supply to the splanchnic area, may attract leukocytes away from the superficial blood, and result in a diminished number of cells when counted by the ordinary methods.

CONCLUSIONS

1. Bottle-fed babies do not constantly show digestive leukocytosis; in fact, the majority show a smaller number of leukocytes in the superficial blood after taking food than before.

2. This decrease is greatest at from one to two and a half hours after food, and tends to rise before the next feeding.

3. When a rise does occur, it is most frequently soon after feeding, and begins to decline in a half-hour.

4. Crying, struggling and chilling of the part from which the blood is extracted increases the count.

5. There seems to be as yet no adequate explanation for the increase or decrease.

6. Comparative counts should be made at the same time of day, and at the same time in relation to food.

I wish to thank Dr. J. C. Gittings and Dr. William Pepper for their valuable advice in the preparation of this work; Dr. Theodore LeBoutillier, Dr. John F. Sinclair and Dr. Arthur Newlin for their kindness in allowing me the use of their cases at the Babies' Hospital.

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