

HEMOREFRACTOMETRY IN INFECTIOUS DISEASES OF CHILDREN *

MELLO-LEITAO, M.D.

Professor of Pediatrics, Medical School of Bello-Horizonte

MINAS GERAES, BRAZIL

Refractometry is yet an almost blank chapter in pediatrics. In contrast to the now numerous papers on refractometry in adults, such researches in children are rare.

On normal refractometry of blood serum in healthy children we know only the papers of Reiss¹ and Nast.² According to Reiss the refractometric index of blood serum in nurslings is lower than in adults, and this decrease agrees with about a 2 per cent. lower concentration of serum proteins. From the age of 6 to 10 months, says Reiss, the refractometric index rises and attains a definite degree, with a value varying from 1.3480 to 1.3514, as in adults. Refractometry is perhaps the best and surest means of serum protein estimation; Reiss's researches on the subject are too well known to need any detailed mention here.

In order to estimate protein concentration in blood serum, we subtract from the number read 1.33320, which is the value of n/D to distilled water, plus 0.00277, corresponding to the other substances in solution in blood serum, and then divide the remainder of the two successive subtractions by 0.00172, the refractometric variation to 1 per cent. protein solution. So if we find $n/D = 1.34872$ to be the refractometric index of a serum, we have $1.34872 - (1.33320 + 0.00277) = 0.01285$, and $0.01285 : 0.00172 = 7.41$, then the protein concentration of this serum is 7.41 per cent.

According to Nast there are in infancy five periods of protein concentration in blood serum, as follows: from 1 to 3 months; from 3 to 8 months; from 8 to 18 months; from 1½ to 5 years and from 5 to 14 years, with a progressive increase, and is the same as that in adults during the last two periods.

In order to have a paradigm for our next following observations, we have estimated blood serum-protein concentration in healthy infants with Abbe's total refractometer. Reiss's and Nast's studies were made with Pulfrich's immersion refractometer, which gives a number of five decimals, while Abbe's refractometer gives only four.

* Submitted for publication, Nov. 9, 1915.

* Read before the Brazilian Society of Pediatrics, Oct. 10, 1915.

1. Reiss: *Jahrb. f. Kinderh.*, lxx.

2. Nast: *Ztschr. f. Kinderh.*, 1914, p. 92.

My results in contrast to those of Reiss and Nast, are as shown in Table 1.

TABLE. 1.—COMPARISON OF REFRACTOMETRIC RESULTS

Age, Months	Reiss		Nast		Mello-Leitão	
	N/D	Proteins, Per Cent.	N/D	Proteins, Per Cent.	N/D	Proteins, Per Cent.
1—	1.34557 to 1.34747	5.6 6.7
	1.34503 to 1.34826	5.26 7.20	1.3449 to 1.3465	5.19 6.12
1	1.34580	5.7	1.34605 to 1.34672	5.69 6.25	1.3463 to 1.3468	6.0 6.29
2	1.34654	6.1	1.34523 to 1.34690	5.96 6.34	1.3461 to 1.3468	5.88 6.29
3	1.34635 to 1.34659	6.0 6.2	1.34540 to 1.34749	5.46 6.70	1.3463 to 1.3472	6.0 6.52
4	1.34721 to 1.34802	6.5 7.6	1.3469 to 1.3472	6.36 6.52
5	1.3470 to 1.3475	6.41 6.58
6	1.34694	6.38	1.3470 to 1.3474	6.41 6.52
7	1.3470 to 1.3478	6.41 6.87
8	1.34676	8.0	1.34695	6.38	1.3469 to 1.3478	6.35 6.87
9	1.34798	6.98	1.3471 to 1.3480	6.47 7.0
10	1.34733	6.6	1.34820	7.10	1.3480 to 1.3485	7.0 7.28
11	1.34779 to 1.34823	6.88 7.12	1.3482 to 1.3500	7.11 8.15
12 to 18	1.34895 to 1.34920	7.5 7.7	1.34854 to 1.35006	7.31 8.18		
18 to 60	1.34894 to 1.35110	7.5 8.8				

The results show infancy to be divided into four periods of albuminemic concentration: Under 3 months, when n/D is below 1.3470; from 3 to 8 months, with n/D varying from 1.3478; from 8 to 18 months with n/D varying from 1.3480 to 1.3485, and over 18 months, with n/D values above 1.3482. Chart 1 shows the refractometric figures of Reiss, Nast and mine.

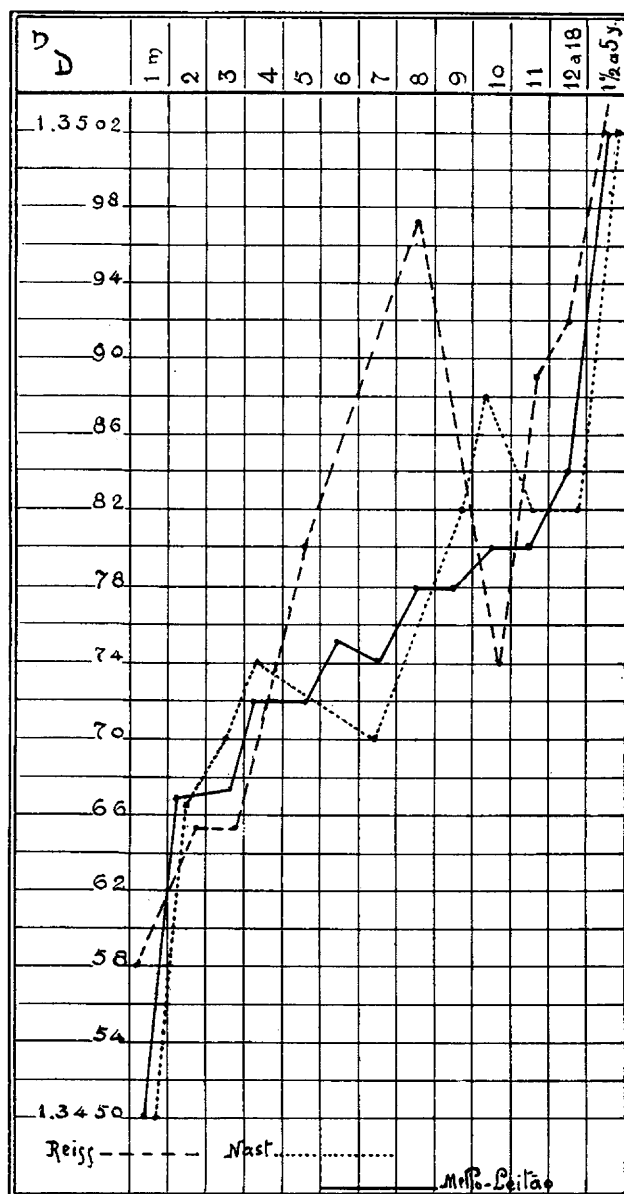


Fig. 1.—Normal refractometric index in infancy.

We have seen that as soon as the child takes table food the refractometric index rises and attains adult values, and this index varies within the same bounds after 18 months.

Refractometry of the blood in infectious diseases has been the subject of papers by Landelowski, Oppenheimer and Reiss, and Achard

and Saint-Girons. Achard, Touraine and Saint-Girons³ in their researches on rheumatism, pneumonia and typhoid fever have shown a very near relation between sickness evolution and serum protein concentration. These authors consider, in the course of an acute infectious disease, four albuminemic phases as follows:

First phase, the percentage of proteins falls more or less regularly;

Second phase, albuminemy decreases to the lowest degree;

Third phase, protein concentration rises slowly or swiftly; and in the

Fourth phase, exceeds the normal degree, descending to it again little by little.

TABLE 2.—PROTEIN CONCENTRATION IN MEASLES

Name	Age, Months	Fever Days	Eruption Day	Koplik	N/D	Proteins, Per Cent.
Olivia.....	10	4	2d	+	1.3452	5.36
Heitor.....	7	3	1st	+	1.3463	6.0
Jandyrá.....	23	4	1st	+	1.3471	6.52
Nair.....	34	3	1st	+	1.3470	6.41
Octavio.....	6	..	3d	—	1.3448	5.12
Dalila.....	18	..	4th	—	1.3470	6.41
Christovão.....	5	..	12th	—	1.3466	6.17
Luiz.....	8	..	25th	—	1.3480	7.0
Heitor.....	36	3 (39 C.) 5 (37.5 C.)	1st	+	1.3475	6.58
			3d	+	1.3463	6.0
			8th	—	1.3485	7.86
			15th	—	1.3503	8.33

In the first phase the albuminemic percentage is directly proportional to the duration and gravity of the infection; thus, in pneumonics whose disease endures from six to nine days, the least percentage of proteins was 7.224; in typhoidics, whose disease protracts itself to twenty days or more, the percentage descends to 6.771. The decrease is at first abrupt, becoming slower as it approaches the minimum, and while there is fever, the protein percentage progressively descends to the minimum and remains there.

In the second phase the refractometric index comes to minimum when the fever falls and the temperature tends to become normal; in

3. Achard, Touraine and Saint-Girons; Arch. de méd. expér. et d'anat. path., 1912, xxiv, 647.

diseases whose fever falls suddenly, the least degree of protein concentration is attained the day or the afternoon of crisis; in lysis, on the last day, when the fever decreases slowly.

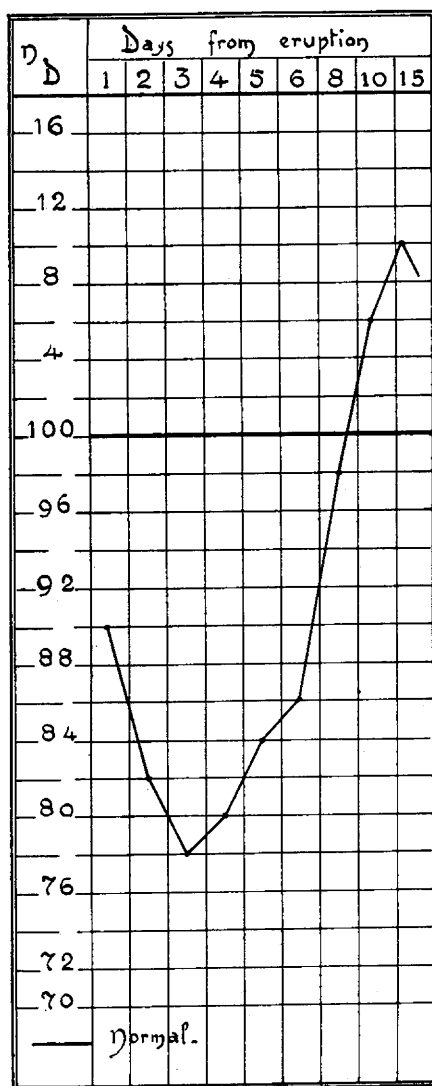


Fig. 2.—Hemorefractometry of measles as compared with the normal.

This second albuminemic phase occurs according to two clinical states. (a) It is only a slight condition, and in figures is represented by an acute angle between the descending line of the first phase and the ascending line of the third; (b) there is a more or less lasting condition,

during which the refractometric degree maintains itself constant, or with very little oscillation; in figures it is represented by a horizontal bar joining the oblique lines of the first and third phases. The first figure is observed when there is crisis, and the second when termination is by lysis.

The protein percentage rises after the day without fever, and in general this ascent is at first slow and afterward more rapid; sometimes the rise is rather sudden (only when there is crisis).

The fourth phase is not constant, but often the protein concentration goes far beyond the normal, and afterwards decreases little by little.

TABLE 3.—REFRACTOMETRIC OBSERVATIONS IN WHOOPING COUGH

Name	Age, Months	N/D	Proteins, Per Cent.	Observations
A. M.	36	1.3472	6.52	Nauseous cough since 6 days.
C. S.	4	1.3455	5.54	Nauseous cough since 3 days.
S. M.	7	1.3490	7.57	Spasmodic cough since 1 month.
S. S.	10	1.3510	8.73	Spasmodic cough since 50 days.
L. F.	11	1.3480	7.00	Spasmodic cough since 75 days.
G. N.	72	1.3489	7.51	Spasmodic cough since 6 months.
J. U.	24	1.3490	7.57	Spasmodic cough since 3 months.
U. F.	3	1.3492	7.69	Spasmodic cough since 40 days.
W. F.	10	1.3490	7.58	Spasmodic cough since 21 days.
H. A.	36	1.3500	8.15	Spasmodic cough since 7 days.
D. A.	24	1.3460	5.83	Nauseous cough 4/18/15.
		1.3488	7.46	Spasmodic cough 5/10/15.
D. C.	48	1.3487	7.40	Spasmodic cough since 10 days.
		1.3503	8.33	Spasmodic cough since 30 days.

The researches of Engel, Sandelowsky, Oppenheimer and Reiss, and Bohme all conform to those of Achard, Touraine and Saint-Girons. According to Reiss⁴ the fall of protein concentration is due to one of three causes: water retention by the organism; absolute decrease of proteins; water carriage from tissues to the blood stream. In pneumonia and scarlet fever, as shown by Oppenheimer and Reiss, refractometric figures are inversely proportional to weight figures; they have seen that in chlorid crises, weight decrease and refractometric index increase come together. Von Leyden had otherwise observed water retention in fever.

4. Reiss: *Ergebn. inn. Mediz. u. Kinderh.*, 1913, xi.

During fever there is a great protein destruction, which is indicated by an increase of nitrogen output. It is probable that the proteins of the blood stream are also raised, but we do not understand that such

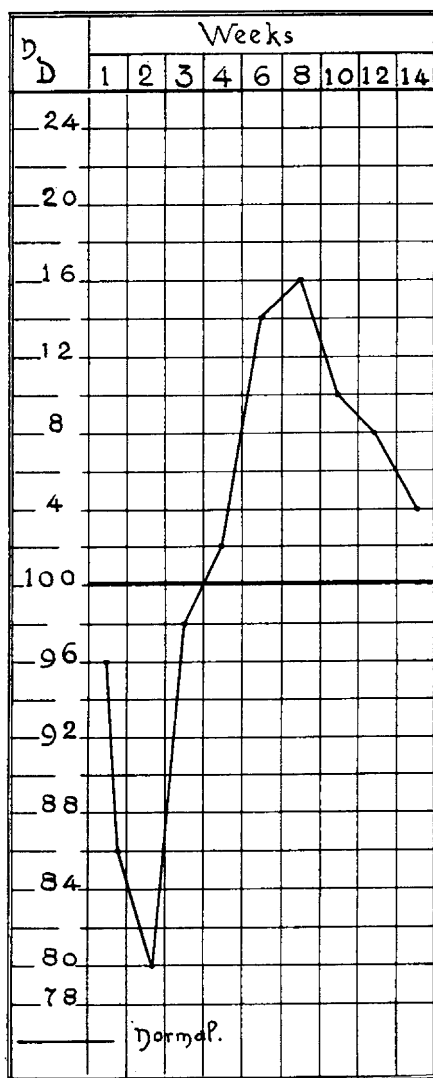


Fig. 3.—Hemorefractometry of whooping cough as compared with the normal.

destruction promotes so great a decrease of protein concentration as that observed. Reiss, however, believes this to be the cause of refractometric index decrease in cases with high fever, weight loss and no chlorid retention.

Water flow from tissues to blood in superwarming was experimentally demonstrated by Sandelowsky, but clinically we observe that fever figures in no way parallel the refractometric figures. In superwarming protein concentration rises forthwith after warming ceases, but in recovery from febrile infections the refractometric index rises little by little. Reiss believes that almost always blood dilution proceeds from water and chlorid retention.

TABLE 4.—REFRACTOMETRIC INDEX IN LATENT AND SURGICAL TUBERCULOSIS

Name	Age, Years	Weight, Gm.	Diagnosis	N/D	Proteins, Per Cent.
D. B.	½	6,500	Latent tuberculosis	1.3460	5.83
E. R.	5/12	8,000	Latent tuberculosis	1.3477	6.81
G. S.	½	6,900	Latent tuberculosis	1.3475	6.70
U. B.	¾	5,000	Adenopathy.....	1.3448	5.13
D. F.	1 1/12	7,200	Adenopathy.....	1.3458	5.71
A. A.	10/12	9,800	Adenopathy.....	1.3468	6.29
A. S.	8	24,900	Adenopathy.....	1.3482	7.11
M. J.	7	16,000	Adenopathy.....	1.3476	6.76
C. S.	7	20,000	Adenopathy.....	1.3478	6.87
V. R. C.	11	29,000	Serous pleurisy....	1.3499	8.09
U. C.	6	13,500	Pott's disease with pulmonary tub.	1.3401	6.47
A. D.	3	13,000	Pott's disease.....	1.3510	8.73
J. J.	7	22,700	Coxalgia.....	1.3507	8.56
A. A.	9	25,000	Coxalgia.....	1.3488	7.46
W. D.	8	24,200	Serofula.....	1.3478	6.87
C. S.	2½	6,300	Pulmonary tubere.	1.3439	4.61
H. T.	1 7/12	5,400	Pulmonary tubere.	1.3449	5.19

It is very interesting to compare the results from observation of infectious diseases and those which have been shown by Widal, Abrami, Brissaud, Benard and Joltrain⁵ in anaphylaxis. They observed sudden fall of the refractometric index, and believe these variations to be due to physicochemic alterations of plasmatic colloids.

In order to see if in infancy refractometric figures were the same as in adults, I have examined serumprotein concentration in infants and children at the Children's Hospital Dispensary at Rio de Janeiro, where I was consulting physician.

I have divided this research into two parts: on acute, and on chronic infectious diseases. Concerning acute diseases, I have found

5. Widal, Abrami, Brissaud, Benard and Joltrain: *Compt. rend. Soc. de biol.*, 1914.

in measles a figure identical with that of Achard, Touraine and Saint-Girons, as I show in the observations of Table 2.

The refractometric index is an excellent aid in the differential diagnosis from rubeola. In this last disease protein concentration suffers no variation as I have observed in the following case:

Ismenia V., 7 months old, had a low fever for three days, with an irregular eruption. Koplik—; Theodor +; fever 37.6 C.; $n/D = 1.3472$. Proteins 6.52 per cent. After four days the value of n/D was the same.

The refractometric index in the course of measles in regard to normal is as shown in Figure 2.

As whooping cough is an apyretic, subacute infection, it was very interesting to ascertain if the Achard, Touraine and Saint-Girons curves were here the same. Researches were made in nauseous and spasmodic periods of the disease and I observed ever a low albuminemy in the first period and a remarkable increase in the last. Table 3 gives a summary of my fourteen observations on this disease.

I have registered in Chart 3 the refractometric index variations from normal in whooping cough.

Refractometry allows here the differential diagnosis from tracheobronchial adenopathy with spasmodic cough. In whooping cough the refractometric index is, during the spasmodic period, very much increased; in tracheobronchial tuberculous adenopathy, on the contrary, it is always decreased.

Concerning chronic diseases, it is very interesting to observe the low refractometric index of tuberculosis in contrast with the high degree of hereditary syphilis. Strauss and Chajes⁶ found in eight cases of tuberculosis results permitting of no conclusions.

Engel⁷ believes the refractometric index to be almost always normal, and says:

A low refraction coefficient must be considered as a poor prognostic sign, inasmuch as it indicates a high degree of disturbance of nutrition. Particularly noticeable is the successive sinking in such cases, in which a rapid progression leads to an early fatal termination.

Nast,² in Salge's clinic, found in tuberculous children the albuminemic coefficient always increased from 0.5 to 3 per cent. I have found a fairly constant decreased refractometric index, which is, in latent and surgical tuberculosis, almost normal, and becoming lower

6. Strauss and Chajes: *Ztschr. f. klin. Med.*, 1910, p. 285.

7. Einen niedrigen Refraktions-koeffizienten müssen wir dagegen als einschlechtes prognostisches Zeichen ansehen, da dieses auf eine hochgradige Störung der Ernährung hinweist. Besonders auffällig ist das successive Sinken in jenen Fällen, in welchen jene rasche Progression in kurzer Zeit zum Exitus führt." *Wien. klin. Wchnschr.*, 1910, p. 1573.

and lower, reaching the minimum in the last periods of the disease, as shown in Table 4.

Concerning syphilis, all our records show an increased albuminemy, as will be seen from Table 5.

TABLE 5.—REFRACTOMETRIC INDEX IN SYPHILIS

Name	Age, Months	Weight, Gm.	Diagnosis	N/D	Proteins, Per Cent.
M. P.	5	6,100	H. S.	1.3499	8.09
T. G.	13	7,500	H. S.	1.3484	7.23
A. A.	10	5,800	H. S.	1.3461	5.88
N. L.	6	6,200	H. S.	1.3495	7.86
L. S.	8	6,500	H. S.	1.3481	7.05
E. C.	7	7,500	Hydrocephalus	1.3505	8.44
J. S.	10	6,900	H. S.	1.3510	8.73
E. V.	5	5,100	H. S.	1.3481	7.05
J. C.	8	5,000	H. S.	1.3505	8.44
J. U.	11	6,600	H. S.	1.3485	7.28
D. L.	8	6,800	H. S.	1.3500	8.15
T. S.	3	4,400	H. S.	1.3480	7.0
D. V.	6	4,600	H. S.	1.3480	7.0
M. S.	5	6,000	H. S.	1.3482	7.11

In the observations in Table 5 we find an exception in A. A., aged 10 months, with only 5.88 per cent. as the value of the blood-serum-protein coefficient. This infant was atrophic (weighing 5,800 gm.), with alimentary decomposition and signs of tuberculous adenopathy.

CONCLUSIONS

1. The refractometric index of blood serum in nurslings is lower than that of the adult, and increases slowly from the first month till the age of 13 to 18 months, reaching then a definite value.

2. Achard, Touraine and Saint-Girons' albuminemic curve is constant in acute infectious diseases of infancy and childhood.

3. The spasmodic period of whooping cough produces high albuminemy, which permits the diagnosis from tuberculous tracheo-bronchial adenopathy.

4. The hemorefractometric coefficient in tuberculosis is generally lower than normal.

5. Syphilis increases remarkably the protein percentage in blood serum.

In conclusion we wish to express our thanks and indebtedness to Dr. Fernandes Figueira, director of the Children's Hospital.