the addition of a small quantity of trypsin, just as the fibrinogen discussed in the introduction.

Summary.

Speaker gives a description of the method of determining proteins in the bloodserum by spreading in a molecular layer. He mentions the results of a series of determinations in which, together with Ir. P. C. BLOKKER he has used the spreading method and that of KJELDAHL. After this the m^2 found can be reduced to mg.

A number of patients have been examined by this method. As an example of various diseases in which too low a protein percentage of the blood, hypoproteinemia, was found, the author describes a case of *starvation edema*, a case of *nephrosis* and a case of essential *hypoproteinemia*. The results are given of determinations of protein, lipoid, cholesterol and inorganic substances of the bloodserum.

A summary is then given of the *consequences* of hypoproteinemia, based on clinical experience.

When the literature about *animal experiments* is consulted we find: that the *diet*, especially the sort of proteins has an evident effect on hypoproteinemia, which is the consequence of loss of plasm in dogs.

Especially serum protein, given per os, causes the blood protein percentage to increase. It also appears that any animal forms a protein depot in the tissues from which — even when it does not get food — the protein of the plasm is rapidly replaced. The blood protein does increase, but now it is the globulin that increases at different immunizations.

The treatment of hypoproteinemia begins with *restriction of the salt percentage* in the diet. When salt is given the edema reappears. A *diet* is chosen with a high protein percentage and especially serum proteins are given. Intravenously great quantities of concentrated *lyophile* serum are injected.

Medicine. — *Determination of serum albumin and globulin by means of spreading.* By E. GORTER and P. C. BLOKKER.

(Communicated at the meeting of December 27, 1941.)

In the laboratory of the children's hospital of the "Academisch Ziekenhuis" at Leiden, albumin and globulin have of late years been determined almost exclusively by means of spreading, as with this method there is the great advantage that the determination can be done with very little serum.

In a manner previously communicated [1]) the number of m^2 is determined that 1 cc of the protein solution occupies under certain circumstances on 0.1 n HCl and this figure is then reduced to the weight percentage of protein by dividing it by the so-called spreading factor, i.e. the number of m^2 that 1 mg protein occupies under those circumstances. 0.90 is used as spreading factor of albumin as well as of globulin. It is a well known fact that the spreading factor of nearly all proteins on 0.1 n HCl is approximately of this magnitude, e.g. 0.90 m^2/mg for casein, 1.00 m^2 for ovalbumin, 1.13 m^2 for haemoglobin, ca 0.90 m^2 for globulin and euglobulin and ca 1.04 m^2 for pseudoglobulin, see a.o. [2]).

In the first publication [1]) about the determination of serum globulin and albumin by means of spreading we found a spreading factor of 0.90—0.95 m^2/mg for albumin, but for globulin the factor was only 0.60—0.62 m^2/mg. After that it seemed worth while again to test the magnitude of these factors very carefully. Therefore we compared the magnitude of the spreading with the quantity of protein calculated from nitrogen determinations by the KJELDAHL method. The nitrogen determinations were made according to the micro-method described in detail by ABDERHALDEN–FODOR [3]) in which air, free from ammonia, is sucked through the solution containing the destroyed substance, and then through 0.01 n HCl.

It was found however that, contradictory to ABDERHALDEN–FODOR's instructions, it was necessary to boil the solution gently. In this way the total nitrogen percentage and the non protein nitrogen percentage of the sera examined were determined. As the separation of albumin and globulin in the spreading method was always made with ammonium sulphate and as this salt has many advantages over other salts sometimes used for this purpose, the nitrogen determinations of the globulins were also made with the globulins obtained by this method of separation. It was therefore necessary completely to remove the ammonium sulphate before the destruction. This was done by the method of CULLEN and VAN SLIJKE [4]), in which the solution is boiled with MgO and 50 % alcohol until all ammonia has disappeared. In order to be able to use as little MgO as possible, the quantity of ammonium sulphate present in the globulin obtained by the separation was determined in some cases and in further experiments more than double the amount of MgO corresponding to this quantity of ammonium sulphate was taken. Control experiments with ovalbumin solutions free from ammonium sulphate proved that the addition of ammonium sulphate had no influence on the ovalbumin nitrogen percentage obtained by the method described.

From the nitrogen percentage of the total protein and of the globulin fraction the total protein resp. globulin percentage was calculated by multiplication by 6.30. The albumin

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[1]) E. GORTER and F. GRENDEL, Biochem. Z., **201**, 391 (1928).
[2]) C. HOOFT, J. de Physiol., **36**, 652 (1938).
[3]) E. ABDERHALDEN and A. FODOR, Z. physiol. Chem., **98**, 190 (1917).
[4]) G. E. CULLEN and D. D. VAN SLIJKE, J. biol. Chem. **41**, 587 (1920).

Human serum No.	Diagnosis	Particulars	KJELDAHL Nitrogen in gr. %				Protein (6.30 × N) in gr. %			Spreading in m^2/cm^3			Spreading factor in m^2/mg		
			Total	Non protein	Tot. protein	Glo-bulin	Total	Glo-bulin	Albu-min (as diff.)	Total protein	Glo-bulin	Albu-min (as diff.)	Total	Glo-bulin	Albu-min
1	Normal		1.222	0.038	1.184	0.353	7.46	2.22	5.24	74.2	20.3	53.9	0.99	0.91	1.03
2	"		1.34	0.034	1.31	0.405	8.2	2.55	5.6	80.9	23.1	57.8	0.99	0.91	1.03
3	"	0.94 gr. % lipoid in serum	1.34	0.037	1.31	0.344	8.2	2.17	6.0	81.9	20.9	61.0	1.00	0.96	1.02
4	"		1.35	0.030	1.32	0.325	8.3	2.05	6.2	80.7	18.5	62.2	0.97	0.90	1.00
5	"	rather much lipoid in serum	1.20	0.033	1.17	0.313	7.4	1.97	5.4	73.1	18.5	54.6	0.99	0.94	1.01
6	"	8.8 mgr. % bilirubin in serum	1.251	0.026	1.225	0.359	7.72	2.26	5.46	76.2	20.6	55.6	0.99	0.91	1.02
7	leucemia ?		0.918	0.085	0.833	0.369	5.25	2.32	2.93	53.8	24.0	29.8	1.02	1.03	1.02
8	chronic rheumatisme	sedimentation ca. 90 mm/cc	0.99	0.026	0.96	0.48	6.1	3.0	3.1	61.8	27.4	34.4	1.01	0.91	1.11
9	tuberculosis peritonei		1.284	0.028	1.256	0.592	7.91	3.73	4.18	74.8	32.7	42.1	0.95	0.88	1.01
10	celiac disease	0.83 gr. % lipoid in serum	1.186	0.032	1.154	—	7.27	—	—	73.9	—	—	1.02	—	—
11	acute enteritis		0.893*	0.024	0.869	0.161	5.47	1.01	4.46	57.4	10.0	47.4	1.05	0.99	1.06
12	tuberculosis of lung		0.909	0.032	0.877	0.414	5.52	2.61	2.91	56.8	24.7	32.1	1.03	0.95	1.10
13	normal		1.22	0.027	1.19	0.32	7.5	2.0	5.5	77.0	18.8	58.2	1.03	0.94	1.06
14	lipodystrophia	cholesterol in serum was normal	1.067	0.028	1.039	0.275	6.54	1.73	4.81	67.2	15.9	51.3	1.03	0.92	1.07
15	nephritis endocarditis		1.26	0.166	1.09	0.47	6.9	3.0	3.9	69.4	28.0	41.4	1.01	0.93	1.06
													1.01	0.93	1.04

*) According to TER MEULEN HESLINGA (Hydrating) 0.905 gr. %.

percentage was taken in the nitrogen determination as well as in the spreading as the difference between the total protein and the globulin percentage. On spreading we took no account of the lipoids in the serum, as firstly their influence can only be slight (see 1) and secondly as it is doubtful whether the spreading of a protein and that of a lipoid are additive.

The details of the method described above are as follows:

1. *Total protein.*

1 cm^3 serum was diluted with 1 % natrium chloride solution to 10 cm^3. The spreading of this was determined on 0.1 n HCl with the aid of a 5 mm^3 pipette. The nitrogen percentage was determined by destroying 2 cm^3 of the diluted serum with 1 cm^3 concentrated sulphuric acid (in triplicate). After the mass was dark brown 0.5 cm^3 30 % peroxyde of hydrogen was added to the hot liquid, after which it was heated. This was repeated twice. After that the ammonia was made free in the apparatus of ABDERHALDEN—FODOR, and determined.

2. *Globulin.*

The separation of globulin and albumin was made by adding 1 cm^3 saturated ammonium sulphate to 1 cm^3 serum, removing the precipitated globulin by centrifuge (10 min. with ca. 4000 revolutions per min.), washing out with semi-saturated ammonium sulphate and dissolving in 1 cm^3 1 % natrium chloride. This process was repeated twice. Finally the globulin solution was diluted to 10 cm^3 with 1% natrium chloride. The separation was made in duplicate. The spreading of the solutions obtained was determined on 0.1 n HCl with the aid of a 5 mm^3 pipette. The nitrogen percentage was determined by boiling twice 4 cm^3 of each solution with 20 cm^3 50 % alcohol and 50 mg. magnesium oxide until with litmuspaper no ammonia could be detected and then destroying and determining the ammonia formed as with the total protein.

3. *Non protein nitrogen.*

1 cm^3 serum was shaken with 8 cm^3 10 % trichloracetic acid. After 10 min. it was filtrated and the nitrogen percentage of twice 3 cm^3 filtrate was determined in the same way as with the total protein.

The table shows the figures obtained. In one case (total nitrogen of serum no. 11) the nitrogen percentage, besides by KJELDAHL's method, was also determined by hydrating with hydrogen and a mixture of asbestos and finely divided nickle according to TER MEULEN—HESLINGA. The figures obtained with these methods which differ fundamentally are well in accordance with each other. The total protein percentage was also determined by the rather rough method of KAGAN [5]) in which the falling time is determined of a drop of serum in a mixture of mineral oil and methyl salicylate, and from the specific gravity found the protein percentage was calculated. The protein percentages obtained by this more or less empirical method were on the average 0.5 % lower than those obtained by the KJELDAHL method.

From the table it is seen that the spreading factor of globulin is 0.93, that of albumin 1.04 and that of total protein 1.01. In some cases the deviations from these averages are rather considerable while the cause cannot be established with certainty. In some cases HOOFT [2]) found even greater deviations for euglobulin and pseudoglobulin, however.

It cannot be said with certainty what is the cause of the very low spreading factor previously found for globulin (0.60—0.62). Undoubtedly the total protein percentage then determined by using a gravimetric method is too high. This is already seen from factor 7 (see 1) by which the nitrogen percentage found by KJELDAHL's method had to be

[5]) B. M. KAGAN, Journ. of clinical Investigation. **17**, 369 (1938).

multiplied in order to bring it in accordance with the protein percentage found by the gravimetric method. Slight deviations from case to case of factor 6.30 which we have taken now are possible, but a value of 7 is certainly too high. The too high value of the total protein percentage gives much too high values for the globulin percentage (this was then determined as the difference between total protein and albumin percentage) and consequently the spreading factor is much too high. This cause, however, is not sufficient to bring the factor found for globulin to the value of 0.93 found now.

Summary.

Serum albumin and globulin were determined by means of nitrogen determinations according to the KJELDAHL method and by means of spreading. Average spreading factors of 0.93 for globulin, 1.04 for albumin and 1.01 for total protein were found.

Physics. — *Meson theories in five dimensions.* By L. ROSENFELD. (Communicated by Prof. H. A. KRAMERS.)

(Communicated at the meeting of January 31, 1942.)

In spite of the attractiveness of its basic idea, the meson field theory of nuclear systems cannot be said to be firmly established in any definite form. Quite apart from the convergence difficulties inherent in any quantum field theory, one is here confronted from the start with a choice between four *a priori* possible types (1) of meson fields: scalar, vector, and the two dual types with respect to spatial reflexions, pseudoscalar and pseudovector. One may then try to examine which choice provides the widest scope for the theory, including not only an account of properties of nuclear systems, but also a theory of β-disintegration, which in particular involves a definite relation between β-decay constants and the mean life time of free mesons. From this point of view, it appears necessary to adopt a particular combination of a pseudoscalar and a vector meson field, characterized by a simple relation between the constants which define the intensities of the nuclear sources of the meson fields (2) (3).

Recently, MØLLER (4) has pointed out that this "mixed theory" presents itself in a very natural way as a *single* type of meson field in a five-dimensional (pseudo-euclidian) space, *viz.* as a five-vector with respect to the group of ordinary five-dimensional "rotations" (of determinant $+1$) [1]. Moreover, such a representation of the mixed theory leads to an essential reduction of the number of arbitrary constants in the source densities of the meson field. The physical interpretation of the fifth coordinate introduces, however, an element of arbitrariness in the theory. One might, as originally proposed by MØLLER, identify the five-dimensional space with DE SITTER's universe, thus suggesting a somewhat unexpected connexion between nuclear forces and cosmological features. An alternative interpretation consists in considering the five-dimensional space as a projective one, according to VEBLEN's original suggestion (5): this has the advantage of permitting a straightforward treatment of the interaction of the mesons and nucleons with the electromagnetic field; a detailed discussion of this possibility has recently been carried out by PAIS (6).

The special position, thus recognized, of the mixed theory as a fundamental type of five-dimensional meson field raises at once the question as to which other types of such fields would also be possible *a priori*. A convenient starting point for discussing this question is provided by the so-called "particle aspect" of meson theory, *i.e.* a linearized form of the field equations, involving a system of matrices subjected to suitable commutation rules (7). In fact, the different possible types of meson fields are then immediately given by the inequivalent irreducible representations of the algebra of these matrices. Thus, in four dimensions, we have essentially [2]) two irreducible representations, of degree 5 and 10 respectively, to which correspond the scalar and the vector type of mesons, or the two dual types, according to the reflexion properties imposed on the wave function (7). Such considerations are readily extended to five dimensions (8), with the following result: there are essentially [2]) four inequivalent irreducible representations of the extended algebra, of degrees 6, 10, 10 and 15, corresponding to a five-scalar, two distinct five-pseudovector and a five-vector type of meson field respectively.

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[1]) This group includes in fact both the Lorentz group and the spatial reflections, provided the latter are associated with a change of sign of the fifth coordinate. More accurately, the "mixed theory" appears as some degenerate or approximate form of the five-vector theory.

[2]) *i.e.* apart from a trivial representation of degree 1.