

South African war. It was furnished by Surgeon-General Townsend, C.B.

TABLE II.—*Showing the Incidence of Typhoid Fever in Lord Methuen's Column at the Modder River, South Africa, from December, 1899, to March, 1900.*

—	Number.	Cases of typhoid fever.	Incidence rate.
Uninoculated	10,981	257	2·3 per cent.
Inoculated	2,535	26	1·0 „

It will be noted that Table II. testifies to a diminution of the incidence rate by more than half during the period of observation. It would seem legitimate, in view of the statistics set forth above and of previous statistics, to infer the continuance of a similarly diminished rate of incidence during the whole of these men's service in South Africa. It will be noted also that this table discloses nothing with regard to the case mortality of the inoculated and uninoculated attacked by typhoid fever. This omission is no doubt due to the fact that the sick were transferred to hospitals at the base and passed out of Surgeon-General Townsend's ken. We may probably, in view of statistics in Table I., *supra*, and of those included in my synoptical table, infer that there was here superadded to the diminution in the incidence rate of typhoid fever also a diminution in the death-rate.

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SOME REMARKS ON 50 CASES OF BILHARZIA DISEASE,

WITH SPECIAL REFERENCE TO THE CHARACTERS OF THE WHITE CORPUSCLES FOUND IN THE BLOOD AND URINE.

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ATTENTION has been drawn by Coles to the presence of an excess of coarse-grained eosinophile leucocytes in the blood of a patient suffering from bilharzia disease. The presence in the Royal Victoria Hospital, Netley, of a large number of cases of this disease in soldiers who had served in South Africa afforded us an opportunity for making further investigations in connexion with this disorder.

Clinical symptoms.—In most of the cases the clinical symptoms were very slight, vague pains in the back being most complained of; only a few of the patients complained of frequent micturition and pain on passing the urine. When blood was passed it was most marked at the end of micturition and nearly all the patients stated that their linen became blood-stained from a drop or so of urine coming away after they had adjusted their dress. None of them complained of any rectal symptoms.

Duration of the disease.—The duration of the different cases examined was from nine months to over two years and according to the patients no improvement had taken place since the onset. Many of them had had various drugs administered without the slightest effect.

Incubation period.—But little can be said with regard to the incubation of the disease; of 14 men of the Argyll and Sutherland Highlanders 12 first noticed the disease in January or February, 1901, while at Rustenburg or in that neighbourhood. This regiment had been at Rustenburg since September, 1900, and its movements before that date were in the Eastern Transvaal.

Period of the year at which the disease first appeared.—An analysis of the data with regard to the season at which the first symptoms of the disease appeared shows that the disorder may probably be contracted at every period of the year.

Possible extension of the disease to other countries.—The circumstance that patients who contracted the disease in South Africa have already been invalidated to Netley from India, Burmah, and Malta, stations hitherto free from the disease, shows that the ova of the parasite must have been

widely disseminated over the globe by soldiers from South Africa, and it may be noted that this is in conformity with the fact that the endemic area of the disease in Africa has been widely extended by the movements of infected soldiers.

Remarks on the differential blood counts.—The films were in each case stained with Leishman's stain. The number of leucocytes counted was in each case at least 300, this number being considered sufficient in view of the large number of cases examined and the grand total of 16,149 leucocytes were counted. The blood of all the patients examined seemed to contain an excess of white cells. With the exception of Case 14 the percentage of coarse-grained eosinophile leucocytes was above the normal limits, the average for the whole series being 16·48 per cent. There were, however, great variations in the different cases, the extremes being Case 2 with 40 per cent. and Case 14 with 1·3 per cent. Of the remaining cases 20 (Nos. 1, 3, 4, 5, 6, 15, 20, 22, 23, 24, 30, 33, 34, 39, 45, 46, 47, 48, 49, and 50) showed a percentage of above 15 and in only two (Nos. 36 and 43) was the percentage below 6. The increase of the eosinophiles seems to have been principally at the expense of the polymorphonuclears. Polymorphonuclear leucocytes were below the average percentage, the average for the series of cases being 44·58 per cent. The general impression was that these leucocytes were distinctly more granular than usual, the granules being both more numerous and of larger size and in some instances almost approached the condition seen in normal guinea-pigs' blood.

The large mononuclear leucocytes were relatively numerous, the average percentage being 12·526. In two cases (Nos. 35 and 42) in which evidences of malaria were found—namely, pigment contained in some of the mononuclears in the former case and both benign and malignant tertian parasites in the other case—the figures were very high, 25 per cent. and 28·4 per cent. respectively; but in ten other cases (Nos. 1, 2, 3, 4, 5, 7, 10, 13, 31, and 39) the percentage was above 15. Many of the mononuclear cells contained a few red-staining granules. Intermediary forms between lymphocytes and large mononuclears were numerous and it was often difficult to know into what category the cell should be placed. Doubtful cells were therefore classed as lymphocytes. Lymphocytes gave an average percentage of 25·76, different cases showing large variations. In only two (Nos. 14 and 43), where the figures were 43·9 per cent. and 42·6 per cent., was there a distinct increase, and in both of these cases the coarse-grained eosinophiles were very much less numerous than usual. Included under the head of basophile were mast cells and their average number (0·503 per cent.) was rather above the average of normal blood. In no case, however, did they reach 2 per cent.

Taking the mononuclear leucocytes as one class and the polymorphonuclears as the other, the average percentages work out at 38·286 per cent. and 61·569 per cent. respectively, this being approximately the proportion found in normal blood.

The urinary sediment.—The urine was in each case centrifuged, one portion of the deposit was examined without staining, another was made into films and lightly stained with Leishman's stain. The number of bilharzia ova varied enormously in different cases and also varied from day to day in the same case, the specimens in which most were found being often comparatively free from both cellular debris and blood. The amount of blood varied enormously—in some cases the urine was bright red, in others nothing was noticeable with the naked eye; many of the cases which contained much blood showed extremely few ova. Bladder epithelium was frequently present.

In all the cases examined the sediment contained many leucocytes which were, as a rule, extremely well preserved; by far the greater number of these were coarse-grained eosinophiles. In some cases no other sort of leucocyte was found after prolonged search and in the cases where they were least numerous this percentage never sank below 50; the other form of leucocyte seen was almost exclusively the polymorphonuclear, lymphocytes and large mononuclears being very uncommon. No explanation could be found for this striking predominance of the eosinophile over the other leucocytes and the only suggestion that can be given is that the irritation arising from the lesion of the bladder causes either the other leucocytes to change into eosinophiles or has some special attraction for this form of cell.

CONCLUSIONS.

1. *Histological characters of the blood.*—(a) The percentage of the coarse-grained eosinophile leucocytes is, with very

TABLE GIVING PARTICULARS OF 50 CASES OF BILHARZIA DISEASE.

No. of case.	Rank.	Regiment.	Place and date where the disease was first noticed.	Place whence patient was invalided.	No. of leucocytes counted in each case.	Percentage of various leucocytes.				
						Eosino- philes.	Poly- morpho- nuclear.	Lympho- cytes.	Large mono- nuclear.	Baso- philes.
1	Private.	2nd Royal Irish Fusiliers.	Machadadorp, April, 1902.	South Africa.	302	16·2	48·0	18·2	15·5	1·9
2	Private.	8th Hussars.	Rustenburg, February, 1903.	"	358	40·0	28·0	11·0	20·0	1·0
3	Private.	Argyll and Sutherland Highlanders.	Rustenburg, February, 1901.	"	336	17·2	38·7	27·3	15·8	0·9
4	Private.	4th King's Royal Rifles.	Daaspoort, November, 1901.	"	323	23·8	33·7	22·0	20·1	0·3
5	Private.	Argyll and Sutherland Highlanders.	Bezoutenhoist Valley, July, 1902.	"	325	7·9	42·8	29·1	19·6	0·4
6	Private.	Royal Horse Artillery.	Zeerust, July, 1901.	"	322	19·2	52·5	17·7	10·9	0·6
7	Private.	1st Argyll and Sutherland Highlanders.	Rustenburg, January, 1901.	"	300	33·0	28·6	21·3	16·0	1·0
8	Private.	2nd East Kent.	Nelspruit, February, 1902.	"	310	13·2	50·6	24·8	9·3	1·9
9	Private.	2nd Duke of Cornwall's Light Infantry.	Koomati Port, May, 1901.	"	331	12·1	39·0	36·2	12·1	0·25
10	Private.	8th Hussars.	Vryheid, October, 1901.	"	332	14·1	45·8	22·0	17·1	1·0
11	Private.	1st Worcesters.	Klerksdorf.	"	312	10·2	38·4	36·2	14·8	0·3
12	Private.	8th Hussars.	Ingogo, October, 1901.	"	306	6·5	50·0	32·3	10·1	1·0
13	Private.	Royal Army Medical Corps.	Rustenburg, November, 1901.	"	306	10·4	41·3	29·5	17·3	1·3
14	Private.	1st Welsh.	Johannesburg, November, 1901.	"	303	1·3	45·2	43·9	9·2	0·3
15	Private.	8th Hussars.	Dundee, November, 1901.	"	321	27·2	31·9	29·4	9·4	0·7
16	Private.	"	"	"	300	7·7	61·6	19·0	11·7	—
17	Private.	1st Royal Fusiliers.	Pretoria, May, 1902.	Burmah.	322	14·6	40·1	35·1	9·0	0·6
18	Private.	2nd East Kent.	Nelspruit, May, 1901.	"	312	19·2	45·0	20·5	14·4	0·6
19	Private.	1st Leicesters.	Standerton, May, 1902.	Madras.	304	14·1	49·3	24·0	12·5	—
20	Private.	1st Durham Light Infantry.	Pretoria, March, 1902.	Wellington.	311	22·8	37·6	25·7	12·8	1·2
21	Private.	1st Royal Fusiliers.	Klerksdorp, June, 1902.	Burmah.	316	17·0	44·3	30·4	7·2	1·0
22	Private.	2nd King's Own Yorkshire Light Infantry.	Pretoria, July, 1902.	Malta.	333	28·2	40·5	24·0	6·9	0·3
23	Private.	1st Royal Fusiliers.	Klerksdorp, August, 1902.	Burmah.	318	19·5	34·1	30·8	14·8	0·6
24	Private.	" "	Klerksdorp, June, 1902.	"	326	28·2	33·8	28·2	9·0	0·9
25	Private.	" "	"	"	305	22·5	41·8	25·9	9·8	0·3
26	Private.	Argyll and Sutherland Highlanders.	Rustenburg, January, 1901.	Calcutta.	309	9·0	66·3	15·2	9·4	—
27	Private.	—	—	—	340	16·9	39·0	30·7	13·0	0·3
28	Private.	2nd Berks.	King Williamstown, July, 1901.	Egypt.	321	12·7	47·9	27·7	11·5	—
29	Private.	Argyll and Sutherland Highlanders.	Rustenburg, February, 1901.	Calcutta.	302	6·8	66·0	20·8	6·0	0·6
30	Private.	1st Durham Light Infantry.	Vryheid, February, 1902.	Wellington.	309	25·8	42·6	17·5	14·2	—
31	Lance-Corporal.	Argyll and Sutherland Highlanders.	Rustenburg, February, 1901.	Calcutta.	331	14·2	45·9	23·8	15·4	9·0

TABLE GIVING PARTICULARS OF 50 CASES OF BILHARZIA DISEASE—(Continued).

No. of case.	Rank.	Regiment.	Place and date where the disease was first noticed.	Place whence patient was invalidated.	No. of leucocytes counted in each case.	Percentage of various leucocytes.				
						Eosino- philes.	Poly- morpho- nuclear.	Lympho- cytes.	Large mono- nuclear.	Baso- philes.
32	Private.	Argyll and Sutherland Highlanders.	Rustenburg, February, 1901.	Calcutta.	316	6.9	55.3	24.3	13.3	—
33	Private.	2nd Berks.	King Williamstown, December, 1900.	Egypt.	333	27.9	43.2	15.6	12.9	0.3
34	Private.	Argyll and Sutherland Highlanders.	Rustenburg, January, 1901.	Calcutta.	335	15.9	56.7	18.4	8.9	—
35	Private.	"	"	"	300	8.3	50.6	16.0	25.0	—
36	Private.	"	"	"	335	5.9	55.2	30.7	7.7	0.3
37	Private.	"	"	"	370	8.6	43.5	36.2	11.6	—
38	Private.	1st Durham Light Infantry.	Brandfort, May, 1902.	Wellington.	345	8.3	60.3	18.5	12.5	0.3
39	Lance-Corporal.	Argyll and Sutherland Highlanders.	Rustenburg, November, 1900.	Calcutta.	378	15.6	46.4	22.6	15.1	0.5
40	Private.	"	Rustenburg, November, 1901.	"	322	8.4	58.0	23.3	9.3	0.9
41	Private.	1st Durham Light Infantry.	Vryheid, March, 1902.	Wellington.	315	12.7	39.6	31.7	15.5	0.3
42	Private.	1st Yorkshire and Lancashire.	Klip River, January, 1902.	Mhow.	310	8.1	35.1	28.1	28.4	0.3
43	Private.	1st West Yorkshire.	Fredricksbad, August, 1901.	Quetta.	312	5.4	46.6	42.6	4.8	0.6
44	Private.	Argyll and Sutherland Highlanders.	Rustenburg, February, 1901.	Calcutta.	350	14.6	44.0	33.1	8.3	—
45	Private.	Liverpool Regiment.	Machadadorp, August, 1902.	Burmah.	354	15.8	49.7	27.9	6.5	—
46	Private.	"	"	"	312	24.3	33.7	31.2	10.1	0.3
47	Private.	Royal Fusiliers.	Klerksdorp, March, 1902.	Mandalay.	333	28.5	37.2	21.3	12.0	0.9
48	Private.	West Yorkshire.	Rustenburg, 1900.	Quetta.	333	17.7	49.5	26.7	5.4	0.6
49	Private.	Royal Fusiliers.	Vryheid, March, 1901.	Burmah.	354	29.6	44.2	12.1	13.8	0.3
50	Private.	East Yorkshire	Klerksdorp, March, 1901.	Mandalay.	317	30.3	30.6	27.5	10.4	0.1

The total number of leucocytes counted was 16,149. The average percentages of various leucocytes were as follows: Eosinophiles, 16.486; polymorphonuclears, 44.58; lymphocytes, 25.76; large mononuclears, 12.526; and basophiles, 0.503.

REMARKS ON URINARY SEDIMENT, &c.

CASE 1.—Ova in the urine were not very numerous. With very few exceptions all the leucocytes in the urinary sediment were coarse-grained eosinophiles.

CASE 2.—Percentages were taken to nearest whole numbers. Ova were very few. All the leucocytes seen in the urinary sediment were coarse-grained eosinophiles.

CASE 3.—Ova were numerous. The leucocytes in the urine were numerous, mostly coarse-grained eosinophiles, but some polymorphonuclears were present.

CASE 4.—Ova were few. All the leucocytes seen in the urinary sediment were coarse-grained eosinophiles.

CASE 5.—Ova were very numerous. The leucocytes in the urine were mostly coarse-grained eosinophiles but polymorphonuclears and lymphocytes were also present.

CASE 6.—Ova were fairly numerous. The leucocytes in the urine were scarce, mostly coarse-grained eosinophiles; some polymorphonuclears were present.

CASE 7.—Ova were scarce. All the leucocytes in the urine seemed to be coarse-grained eosinophiles.

CASE 8.—Ova very numerous. Nearly all the leucocytes seen in the urinary sediment were eosinophiles; a few polymorphonuclears were present.

CASE 9.—One myelocyte was seen. Ova were fairly numerous. The leucocytes in the urine consisted of equal numbers of eosinophiles and polymorphonuclears; much bladder epithelium was present.

CASE 10.—Ova were fairly numerous. Leucocytes in the urinary sediment consisted for the most part of eosinophiles.

CASE 11.—Ova were extremely numerous. The leucocytes in the urine were mostly eosinophiles but some polymorphonuclears were present.

CASE 12.—Very few ova were present in the urine.

CASE 13.—Ova were scarce; there was much blood in the urine.

The leucocytes were not very numerous and were mostly eosinophile, but some polymorphonuclears were present.

CASE 14.—Ova were scarce.

CASE 15.—Ova were fairly numerous. The leucocytes in the urine were mostly eosinophiles.

CASE 16.—Ova were very numerous. The leucocytes in the urine consisted almost entirely of eosinophiles.

CASE 17.—Two myelocytes were seen. Ova were very scarce and much blood was present. The leucocytes in the urine consisted of equal numbers of eosinophiles and polymorphonuclears. Examination of another sample of the urine showed many ova and but little blood.

CASE 19.—Ova were very scarce. Nearly all the leucocytes seen in the urine were eosinophiles.

CASE 23.—Ova were in moderate number. A very large proportion of the leucocytes found in the urine were eosinophiles.

CASE 35.—Some of the large mononuclears contained pigment granules due to malaria.

CASE 40.—The patient was recovering from an attack of orchitis.

CASE 42.—Benign and malignant tertian malaria parasites were present in the blood.

CASE 45.—There were very few ova. Eosinophiles and polymorphonuclears were present in about equal proportions in the urinary sediment; a very few lymphocytes were seen.

CASE 47.—Very few ova were present. The eosinophiles were slightly more numerous than the polymorphonuclears. A very few lymphocytes were seen.

CASE 48.—Very few ova were present. The leucocytes were mostly eosinophiles, the remainder being polymorphonuclears with a very few lymphocytes.

CASE 49.—Very few ova were present. The leucocytes were almost all eosinophiles.

CASE 50.—Very few ova were present. The leucocytes were largely eosinophiles.

few exceptions, much above the average percentage found in normal blood. (b) This increase goes hand in hand with a proportional diminution in the percentage of the polymorphonuclear leucocytes. (c) Less frequent is an increase of the large mononuclear leucocytes, and where this is present it is associated with a diminution of the lymphocytes.

2. *Histological characters of the white blood corpuscles in the urinary sediment.*—A very large proportion of the leucocytes found in the urinary sediment are coarse-grained eosinophiles, the remainder being almost all polymorphonuclears, lymphocytes and large mononuclear leucocytes being uncommon.

3. *Variations in the number of ova in the urine.*—The ova vary in number greatly from day to day; large quantities of blood and other cells are often present when but few ova can be found.

SOME INVESTIGATIONS ON THE URINE OF CHILDREN.

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THE object in writing this paper is threefold: firstly, to estimate the average amount of urine passed in 24 hours by children of average health of the ages of six months up to 12 years inclusive; secondly, the estimation of the total urea usually passed in the urine of children when in health; and thirdly, the quantitative estimation of the purine bodies in the urine of children of the ages mentioned. The results obtained are recorded in a table and are in relation to age and to body-weight. A full and complete record of the diet has been kept during each experiment. The great bulk of the cases were taken from healthy workhouse children belonging to the parish of Lambeth, but a few cases were taken from the Royal Hospital for Children and Women, Waterloo-road, S.E. (only those beyond suspicion of disease being selected), and three of the children were private patients. The mode of procedure adopted in order to obtain the samples and to arrive at the estimation of the total urine passed by the child in the 24 hours was as follows. The child was required to empty the bladder at a given time—say, 12 noon. This sample was not saved, but all the urine passed up to, and including that passed at, the same hour next day was kept, well mixed, and a sample taken of the mixed urine. The urine total was measured and recorded in cubic centimetres. Each child was also carefully weighed at the time of the experiment. Urea is the chief nitrogen-containing constituent of the urine and its amount was ascertained by means of Gerrard's ureometer, all urine containing albumin being rejected except one sample which contained a very slight trace; this was boiled and carefully filtered before being tested. The purine bodies, although containing a comparatively small quantity of nitrogen, are of great interest from the point of view of proteid metabolism and the estimation of uric acid and I am not aware that they have been estimated systematically and in this manner before. The purine bodies used to be called xanthine bases or nuclein bases because they are derived from nuclein, or alloxuric bases because they contain in combination two radicles, one of alloxan and the other of urea. Latterly they have been shown to be derivatives of a substance called purine by E. Fischer. They consist of the following amongst others (purine $C_5H_4N_4$): monoxypurine or hypoxanthine, $C_5H_4N_4O$; dioxypurine or xanthine, $C_5H_4N_4O_2$; amido-purine or adenine, $C_5H_4N_4NH$; amido-oxypurine or guanine, $C_5H_4N_4ONH$; trioxypurine or uric acid, $C_5H_4N_4O_3$. Theobromine (dimethyl xanthine), caffeine theine (trimethyl xanthine), substances which are present (in quantities varying from 1 to 3 per cent.) in cocoa, coffee, and tea respectively, are also purine derivatives. Purine itself ($C_5H_4N_4$) has not as yet been discovered in the body.

The quantity of purine bodies found in the urine bears a direct relation to the amount of the purine contained in the food eaten and is also affected by the extent of the nuclein cleavage in the metabolic processes of the body. The former group have been named exogenous and the latter endogenous purine. The purine bodies may be fully precipitated by

nitrate of silver in ammoniacal solutions or by cuprous oxide in the presence of sodium bisulphite. They exist in all forms of meat extracts and in flesh meats of all kinds. The potato and other vegetables, such as the beetroot, contain them. Oats also contain them. The specific actions of uric acid and the other purine bodies upon the various tissues of the body are of great interest and importance: (1) in relation to the question of diet in children during the early years of life; and (2) in regard to the cessation of the processes of growth, the maintenance of adult life, and the gradual decline of bodily activities.

The estimation of purine substances in food has been made by several observers—Kossel-Burian and Schur, Offer and Rosenquist, and more recently by Dr. I. Walker Hall of Manchester. Several methods have been devised for the estimation of uric acid which need not be described here. The method of Dr. Hall for estimating the total urinary purines is one which I have used and is as follows. (In the experiments recorded in this paper only albumin-free urine was used, but for other experiments if any albumin should be present it is necessary to precipitate and to remove it by filtration.) Two solutions are used:—No. I. solution consists of Ludwig's magnesium mixture,¹ 100 cubic centimetres; ammonia solution, 20 per cent., 100 cubic centimetres; and talc, 10 grammes. No. II. solution consists of silver nitrate, one gramme; ammonia, strong, 100 cubic centimetres; talc, five grammes; and distilled water, 100 cubic centimetres. To 90 cubic centimetres of the urine 20 cubic centimetres of No. I. solution are added. An immediate precipitate of the phosphates falls and the clear fluid remains. To 80 cubic centimetres of the clear fluid 18 cubic centimetres of solution No. II. are added. The resultant precipitate is a mixture of silver chloride and silver purine. The former body is dissolved by the excess of ammonia. The filtrate is shaken until all white flakes disappear and the finely granular yellow-white precipitate remains suspended. If the silver chloride is not entirely dissolved strong ammonia is added drop by drop and the solution well shaken until no AgCl remains. These two processes which have first been described are best carried out by means of the "purinometer." It consists of three parts: (1) a closed graduated tube, (2) a stop-cock with above of the same diameter as the upper tube, and (3) a small glass reservoir of known cubical capacity. The graduated tube is capable of being shut off from the broader part by the glass stop-cock. The upper part of the cylinder has a moveable glass-stopper. 90 cubic centimetres of urine are taken from the mixed urine of the 24 hours and poured into the graduated cylinder, taking care to have the stop-cock turned off. Solution I. is added and the resulting precipitate of phosphates is allowed to fall into the lower part of the tube by turning on the stop-cock. The time for the fluid to become quite clear varies, but is never less than five minutes and seldom over half an hour; the powdered talc greatly helps the precipitate to settle. When the phosphates have in this manner fallen to the lower end of the tube the stop-cock is turned off again and No. II. solution is added up to 100 cubic centimetres. The purinometer should be inclined vigorously backwards and forwards for about a minute in order to dissolve the silver chloride and to reduce the flakes to a finely divided precipitate. The apparatus is placed in a cupboard away from the light and then the number of cubic centimetres occupied by the precipitate is read off 24 hours later. Dr. Hall recommends waiting as long as this and I have followed these instructions, but I consider that this time is unnecessarily long. No tea or coffee was allowed during the experiment. Table I. shows the results which were obtained by the methods which have just been indicated.

This table gives a summary of the results of these investigations. It has been shown that in order to obtain reliable information regarding the amount of urine, urea, or purine bodies it is not sufficient to take one 24 hours' sample, at least three must be taken from each case. The variation is often considerable from day to day and the urea which on one day shows a high percentage on the following day (and perhaps because of this) may have dropped to a corresponding low ratio. This remark also applies to the amount of urea, which in many cases varies very considerably on different days, and the same applies to the purine estimation. In all, 63 samples have been taken from healthy children, so that the results have some claim to be regarded as fairly

¹ Mag. chlor. crystal, 110 grammes; ammonium chloride, 110 grammes; ammonia, 250 grammes; and water, one litre.