THE BRITISH JOURNAL OF DERMATOLOGY AND SYPHILIS

DECEMBER, 1920.

ABSORPTION AND ELIMINATION OF MERCURY IN THE DIFFERENT METHODS USED IN THE TREATMENT OF SYPHILIS.

SVEND LOMHOLT, M.D.,

Head of the Department for Skin and Venereal Diseases, Royal Danish Marine
Hospital, Copenhagen.

OUR experience tends to prove that the therapeutic result of any particular mercurial treatment depends entirely upon the quantity of mercury absorbed and brought in circulation and upon the regularity of this absorption. The chemical character of the mercury compound used is but of slight consequence if only the compound can be easily decomposed in the body.

Certain aromatic compounds cannot—or can only partially—be decomposed, and consequently their therapeutic effect is correspondingly diminished.

The rapidity of elimination depends mainly upon the rapidity of absorption, and can be studied by quantitative analysis of the excretions of the body, *i. e.* urine and fæces. The sweat contains only minute quantities of mercury, and the same is the case with the saliva, which, moreover, is chiefly swallowed. The expired air contains no mercury.

The rapidity of the absorption of intramuscularly injected mercury can also be studied directly on animals by isolating the foci of injection and determining their content of mercury at different intervals.

ANALYTICAL METHOD.

The main difficulty in these researches comes from the extreme smallness of the quantities that have to be determined. Very often a litre of urine contains only a few tenths of a milligramme. In the literature I have found no less than fifty-eight different methods, but none of these possesses a sufficient sensitiveness or reliability. I have therefore devised a new analytic method, assisted by J. A. Christiansen, lecturer at the Royal Institute of Chemistry in Copenhagen. This method possesses an exactness to 0.03 mgrm.

A litre of urine is boiled with 100 c.c. H_2SO_4 and to it an excess of KMnO_4 is added. The precipitate is removed by oxalic acid, and 0.25 grm. of CuSO_4 is added. This copper and with it any mercury present is precipitated by H_2S , and the precipitate is isolated by a fine filter of asbestos. Afterwards the precipitate is dissolved in 3 c.c. of HNO_3 (50 per cent.) containing 1 per cent. of hydrochloric acid. 20 c.c. of water is added, and now the mercury is precipitated by electrolysis upon a small thin gold plate (0.05 grm.). The E.M.F. to be used is limited to 1.35–1.45 volts. With this tension all the mercury but no copper is precipitated. After the electrolysis is completed the electrodes are carefully desiccated, weighed on a "Nernst" balance, heated to red heat in a current of hydrogen and then weighed again.

Fæces and solid tissue are to be treated in advance by fuming nitric acid.

By this method an analysis can be undertaken in two hours. I have myself made about 1000 observations.

I have taken a special interest in the examination of the elimination by the intestine. Most authors consider this the chief way of elimination, though only very few examinations have been made on this subject in spite of the great importance of the question in the estimation of the retention of the metal in the body after a cure. A considerable number of examinations of elimination by the kidneys have previously been made.

In opposition to this I found in over 300 cases that only very seldom did the quantity of mercury in the fæces exceed that in the urine, and usually it was only $\frac{1}{6}$ – $\frac{1}{3}$ of the total quantity eliminated. This simply means that we must reckon on a much greater retention of mercury than we had suspected.

INUNCTION TREATMENT.

In Denmark this form of treatment remains the treatment of choice, especially in the hospitals. It works in a regular, reliable and effective way. The quantity of ointment used varies from 3-5 grm. The effect obtained increases according to the quantity of ointment, the surface of skin treated by it and the intensity of the inunction. The elimination of mercury under a treatment by 3 grm. of ointment per day was studied in two patients for thirty-eight and forty-five days respectively. The total quantity of urine and of fæces was examined every day. In both cases a slow but regular increase of the elimination was observed during the first three weeks. Afterwards the elimination kept almost stationary at about 3 mgrm. per day. Details can be studied on the tables (I and II). A third series of examinations showed that even forty days after the stopping of the treatment the elimination exceeded 0.5 mgrm. per day.

The average elimination per day under treatment was 2.17 and 2.15 mgrm. The quantity eliminated in the fæces amounted to 26.2 and 30.8 per cent. of the total, but this elimination was very irregular and without any remarkable increase under treatment.

INTERNAL TREATMENT, ETC.

Internal treatment has always been looked upon as feeble and rather unreliable. As the elimination by the intestine cannot be studied under this sort of treatment I have only made a small number of examinations, and the result was always very small. The same has been the case with some examinations of the elimination under a treatment by inhalation of mercury vapours.

TREATMENT BY INJECTIONS.

This treatment has many great advantages. It is easy for the doctor to carry out, and in most cases also comfortable for the patient. It is growing more and more prevalent. Its drawbacks are its occasional—and inevitable—painfulness and often the irregular absorption of the injected material, which may produce in some cases intoxication, in other cases an absence of effect. The character of the effect obtained varies very much with the character of the compounds of mercury used, and depends especially upon the rapidity with which absorption takes place.

TABLE I.—*Inunction Treatment, I.*

EXPLANATION OF THE TABLES.

- 1.—Urine. The hatched area indicates the elimination of mercury (in milligrammes), the clear area the quantity of urine passed (in cubic centimetres).
- 2.—Fæces. The hatched area indicates the elimination of mercury (in milligrammes), the clear area the quantity of fæces (in grammes).
- 3.—Total elimination of mercury (in milligrammes). The lower shaded area indicates the elimination in the urine, the upper that in the fæces. On days where no motion has taken place the result of the next following day has been bisected, and half given to the preceding day.

TABLE II.—*Inunction Treatment, II.*

For explanation of figures see Table I, p. 356.

We can distinguish especially three different sorts of compounds: compounds soluble in water, compounds insoluble in water, and metallic mercury. Several aromatic compounds which cannot be decomposed in the organism possess a special position. As a general rule it may be said that soluble compounds are absorbed rapidly, insoluble more slowly, and metallic mercury still more slowly. Several other factors may also influence the rapidity of absorption. Concentrated solutions (including emulsions) are absorbed a little more slowly than the feeble ones. Emulsions in paraffinum liquidum are absorbed a little more slowly than those in the different vegetable oils. Subcutaneous injections are absorbed considerably more slowly than intramuscular, etc.

COMPOUNDS SOLUBLE IN WATER.

No special difference between these compounds has been observed, as the histological reactions of tissue almost exclusively depend upon the free Hg.-ions present in the mixture.

I have worked with a 2 per cent. solution of hydrargyrum benzoicum (43.5 per cent. Hg.) Thus:

Hydrargyrum benzoicum	.	2	gram.
Natrium chloricum	.	1	„
Saccharum	.	5	„
Aqua destillata ad	.	100	c.c.

Intramuscular injections of 5 c.c. of the solution (0.1 gram. of the salt) were given once a week, in order to obtain a more distinct picture of the curve of elimination than could be the case in using the usual daily injections of small quantities.

Two patients especially were studied for thirty-four and forty days respectively. The detailed results can be seen upon the tables (III and IV). On the day following an injection a marked elimination (about 5 mgrm. Hg., in one case 12.32 mgrm.) was produced. The next days the elimination decreased gradually and more or less regularly to 1-2 mgrm. on the last day before a fresh injection, which caused a new rise in elimination. After the first injection the elimination was usually rather small (studied in five cases). Probably the organism ought to be saturated by mercury in advance. These fluctuations can only be seen in the elimination by the urine. In the faeces only 21.4 per cent. (in both cases) of the total eliminated

quantity was found, and the fluctuations of the elimination have here been quite irregular. Of the total quantity of mercury injected 48·8 and 35·3 per cent. have been eliminated under the treatment itself.

Further direct investigations on absorption and elimination were made on a rabbit, to which six injections of 0·75 c.c. of the solution (6·3 mgrm. Hg.) were given at short intervals.

ABSORPTION IN THE MUSCLES.

Date of the injections.	Injected Hg. in mgrm.	Quantity of Hg. found.	Quantity of Hg. absorbed.
Dec. 28	ca. 6·3	0·40	ca. 5·90
" 30	" 6·3	2·11	" 4·19
Jan. 4	" 6·3	3·21	" 3·09
" 6	" 6·3	3·78	" 2·52
" 7	" 6·3	5·20	" 1·10
" 8	" 6·3	6·00	" 0·30
Total	ca. 37·8	20·70	ca. 17·10

ELIMINATION.

Date.	Injected Hg. in mgrm.	Urine in c.c.	Hg. found in the urine (mgrm.).	Fæces (grm.)	Hg. found in the fæces (mgrm.).	Total quantity of eliminated Hg. (mgrm.).
Dec. 28	6·3	—	—	—	—	—
" 2	—	110	0·21	30	0·31	0·52
" 30	6·3	310	0·43	7	0·14	0·57
" 31	—	60	0·15	15	0·16	0·31
Jan. 1	—	4	0·05	8	0·11	0·16
" 2	—	140	0·16	10	0·08	0·24
" 3	—	280	0·32	15	0·14	0·46
" 4	6·3	190	0·25	8	0·16	0·41
" 5	—	160	0·23	20	0·23	0·46
" 6	6·3	170	0·39	23	0·23	0·62
" 7	6·3	80	0·34	1	0·05	0·39
" 8	6·3	190	0·42	3	0·09	0·51
" 8	—	45	0·81	—	—	0·81
(passed						
" 8	under	80	0·64	2	0·11	0·75
narcosis.)						
Total			4·40		1·81	6·21

CIRCULATION OF HG.

Injected quantity of Hg.	Mgrm.
	37·8
Eliminated by kidneys and intestine	6·21
Hg. found in the viscera	3·14
" " " muscles	20·70
" " " rest of the body	4·8
	34·85

TABLE III.—*Hydrargyrum benzoicum*, I.

For explanation of figures see Table I, p. 356.

TABLE IV.—*Hydratgyrum benzoicum*, II.

For explanation of figures see Table I, p. 356.

Quantity of Hg. lost in the experiment 2.95 mgrm., or 8 per cent. of the injected quantity.

COMPOUNDS INSOLUBLE IN WATER.

Of these, *hydrargyrum salicylicum* and *calomel* are the most frequently used and have both been studied.

Hydrargyrum salicylicum is not a compound of the same sort as the preceding, which is simply a salt of an organic acid. Also it contains much more mercury (58 per cent.). In fact it is an anhydride of the acidum ortho-oxy-mercuri-salicylicum, in which only one of the two valencies of the divalent mercury has been connected to the carboxyl of the acid. The other one is directly connected to the carbon of the benzene nucleus.* This produces a compound very difficult of decomposition. H_2S colours it only very slowly. This fact is of an immense importance for its practical therapeutic use, but in spite of this it seems very seldom to have been taken into account. Undoubtedly we must reckon that a considerable quantity of the remedy can be eliminated without being decomposed in the body.

Two patients were studied for twenty-two and thirty days respectively. Usually an injection of 8 cgrm. was given every fifth day, sometimes a somewhat smaller injection. The detailed results of elimination can be studied on the tables (V and VI).

The scheme of elimination was much the same as that of *hydrargyrum benzoicum*, but the fluctuations of the curve were larger, more abrupt and more irregular. Also here the fluctuations were seen in the urine only. The total elimination in the fæces amounted to 25.5 and 18.8 per cent. of the total, and was quite irregular. Of the injected mercury 38.6 and 49.4 per cent. was eliminated under the treatment itself.

Direct investigations were made on a rabbit, in which injections were given as follows:

* The formula of construction is this:

ABSORPTION IN THE MUSCLES.

Date of injection.	Quantity of Hg. injected.	Quantity of Hg. found in the muscles.	Quantity of Hg. absorbed.
Oct. 7 .	ca. 4.4 .	0.10 .	ca. 4.30
„ 9 .	„ 4.4 .	— .	„ 4.40
„ 11 .	„ 5.8 .	1.12 .	„ 4.68
„ 13 .	„ 5.8 .	0.81 .	„ 4.99
„ 15 .	„ 7.3 .	5.41 .	„ 1.89
„ 16 .	„ 5.8 .	4.10 .	„ 1.70
Total	ca. 33.5	11.54	ca. 21.96

ELIMINATION.

Date.	Injected Hg. (mgrm.).	Urine (c.c.).	Hg. found in the urine.	Fæces (grm.).	Hg. found in the fæces (mgrm.).	Total quantity of eliminated Hg. (mgrm.).
Oct. 7 .	4.4 .	— .	— .	— .	— .	—
„ 8 .	— .	325 .	0.63 .	20 .	0.05 .	0.68
„ 9 .	4.4 .	250 .	0.41 .	24 .	0.31 .	0.72
„ 10 .	— .	220 .	1.63 .	28 .	0.38 .	2.01
„ 11 .	5.8 .	215 .	1.44 .	12 .	0.13 .	1.57
„ 12 .	— .	190 .	0.52 .	12 .	0.48 .	1.00
„ 13 .	5.8 .	100 .	0.42 .	24 .	0.29 .	0.71
„ 14 .	— .	210 .	0.63 .	30 .	0.41 .	1.04
„ 15 .	7.3 .	310 .	0.67 .	30 .	0.33 .	1.00
„ 16 .	5.8 .	90 .	0.72 .	8 .	0.43 .	1.15
Total			7.07		2.81	9.88

CIRCULATION OF Hg.

Injected quantity of Hg.	Mgrm.
	33.5
Eliminated by kidneys and intestine	9.88
Hg. found in the viscera	3.10
„ „ „ muscles	11.54
„ „ „ rest of the body	6.4
	30.92

Quantity of mercury lost in the experiment 2.6 mgrm., or about 8 per cent. These results show also an absorption and elimination which is very rapid and somewhat irregular.

CALOMEL.

Two patients were studied for thirty-two and twenty-five days respectively. They were given injections of 5 cgrm. every fifth day of an emulsion, thus :

Calomel, vapore paratum	10 grm.
Adeps lanæ	5 „
Oleum camphoratum ad	50 c.c.

TABLE V.—*Hydrargyrum salicylicum*, I.

For explanation of figures see Table I, p. 356.

TABLE VI.—*Hydrargyrum salicylicum*, II.

For explanation of figures see Table I, p. 356.

The scheme of elimination was much the same as that in the treatment by inunctions. The single injections produced no effects upon the curve, which rose gradually and more or less regularly. Details can be studied on the tables (VII and VIII).

The elimination in the faeces amounted to 33.5 and 22.4 per cent. of the total elimination and was more or less regular.

Of the injected quantity of mercury 25.1 and 21.5 per cent. was eliminated under the treatment.

A direct investigation on a rabbit gave the following results :

ABSORPTION IN THE MUSCLES.

Date of injection.	Quantity of Hg. injected.	Quantity of Hg. found in the muscles.	Quantity of Hg. absorbed.
Jan. 11 .	ca. 8.0 .	3.1 .	ca. 4.9
„ 14 .	„ 8.0 .	4.3 .	„ 3.7
„ 16 .	„ 8.0 .	3.8 .	„ 4.2
„ 18 .	„ 8.0 .	4.6 .	„ 3.4
„ 19 .	„ 8.0 .	4.6 .	„ 3.4
„ 20 .	„ 8.0 .	5.9 .	„ 2.1
Total	ca. 48.0	26.3	ca. 21.7

ELIMINATION.

Date.	Injected Hg. (mgrm.).	Urine (c.c.).	Hg. found in the urine (mgrm.).	Faeces (grm.).	Hg. found in the faeces (mgrm.).	Total quantity of eliminated Hg. (mgrm.).
Jan. 11 .	8.0 .	— .	— .	— .	— .	—
„ 12 .	— .	45 .	0.11 .	25 .	0.15 .	0.26
„ 13 .	— .	100 .	0.18 .	15 .	0.13 .	0.31
„ 14 .	8.0 .	100 .	0.23 .	20 .	0.10 .	0.33
„ 15 .	— .	200 .	0.32 .	15 .	0.16 .	0.48
„ 16 .	8.0 .	110 .	0.34 .	5 .	0.15 .	0.49
„ 17 .	— .	80 .	0.42 .	6 .	0.10 .	0.52
„ 18 .	8.0 .	90 .	0.40 .	7 .	0.23 .	0.63
„ 19 .	8.0 .	No urine		3 .	0.16 .	0.16
„ 20 .	8.0 .	60 .	0.64 .	2 .	0.13 .	0.77
„ 20 .	— .	110 .	0.41 .	2 .	0.12 .	0.53
Total			3.05		1.43	4.48

CIRCULATION OF Hg.

Injected quantity of Hg.	Mgrm.
	48.0
Eliminated by kidneys and intestine	4.48
Hg. found in the viscera .	1.64
„ „ „ muscles .	26.30
„ „ „ rest of the body .	6.4
	38.82

Quantity of mercury lost under the experiment 9.2 mgrm., or 19 per cent. These results show also an absorption and elimination which is rather slow but regular.

OLEUM CINEREUM.

One patient was treated for thirty-two days by injections of 10 cgrm. mercury of a 50 per cent. emulsion every fifth day.

The curve of elimination was very surprising. In the first fourteen days only small quantities of mercury were eliminated, under 1 mgrm. per day, then a sudden increase occurred and for six days more than 5 mgrm. per day was eliminated. Though the treatment was continued the elimination now quite unexpectedly decreased rapidly, and after another eight days again 1 mgrm. per day only was eliminated (Table IX).

The elimination in the fæces was very irregular and amounted to only 18.6 per cent. of the total elimination. Of the quantity of mercury injected only 9.6 per cent. was eliminated under the treatment.

Some months after the treatment the patient suddenly got a severe mercurial intoxication under hard bodily work and without having received any sort of treatment after that mentioned above. The explanation of these extraordinary observations must be that this remedy—owing to the feeble reaction of metallic mercury on the muscular tissues—was absorbed only very incompletely, and that the bulk had been encapsuled in the muscles.

A direct investigation on a rabbit gave the following results :

ABSORPTION IN THE MUSCLES.

Date of injection.	Quantity of Hg. injected.	Quantity of Hg. found in the muscles.	Quantity of Hg. absorbed.
Jan. 20	ca. 22.0	13.8	ca. 8.2
" 23	" 22.0	14.8	" 7.2
" 26	" 22.0	14.1	" 7.9
" 29	" 22.0	16.3	" 5.7
Feb. 1	" 22.0	18.8	" 3.2
" 4	" 22.0	18.7	" 3.3
" 5	" 22.0	19.7	" 2.3
Total	ca. 154.0	116.2	ca. 37.8

TABLE VII.—*Calomel, I.*

For explanation of figures see Table I, p. 356.

TABLE VIII.—*Calomel, II.*

For explanation of figures see Table I, p. 356.

ELIMINATION.

Date.	Injected Hg. (mgrm.).	Urine (c.c.).	Hg. found in the urine (mgrm.).	Fæces (grm.)	Hg. found in the fæces (mgrm.).	Total quantity of eliminated Hg. (mgrm.).
Jan. 20	22.0	—	—	—	—	—
" 21	—	90	0.05	8	0.05	0.10
" 22	—	240	0.05	15	0.05	0.10
" 23	22.0	250	0.11	10	0.08	0.19
" 24	—	200	0.17	20	0.12	0.29
" 25	—	220	0.28	15	0.14	0.42
" 26	22.0	200	0.21	12	0.13	0.34
" 27	—	40	0.36	20	0.23	0.59
" 28	—	40	0.42	4	0.21	0.63
" 29	22.0	20	0.30	2	0.17	0.47
" 30	—	190	0.33	6	0.14	0.47
" 31	—	250	0.38	12	0.13	0.51
Feb. 1	22.0	300	0.51	÷	÷	0.51
" 2	—	250	0.62	4	0.08	0.70
" 3	—	350	0.58	1	0.05	0.63
" 4	22.0	400	0.72	$\frac{1}{2}$	0.03	0.75
" 5	22.0	210	0.67	3	0.03	0.70
" 6	—	250	0.81	4	0.12	0.93
Total			6.57		1.76	8.33

CIRCULATION OF MERCURY.

Injected quantity of Hg.	Mgrm.
	154.00
Eliminated by kidneys and intestine	8.33
Hg. found in the viscera	1.55
" " " muscles	116.2
" " " rest of the body	11.9
	137.98

Quantity of mercury lost under the experiment 16 mgrm., or about 11 per cent. These results show also a very slow, but in this case more or less regular absorption.

THERAPEUTIC CONCLUSIONS.

It has been discussed widely whether mercury in the infected body acts directly upon the spirochaetes or more indirectly on the human organism by stimulating the bactericidal forces in it. Of these theories the latter is to be preferred in my opinion. Eighteen examinations of blood from patients under full mercury treatment or

TABLE IX.

Oleum cinereum.

For explanation of figures see Table I, p. 356.

severely intoxicated with this metal have shown me that the average content of mercury amounts to 1-2 mgrm. only per litre and never exceeds 3 mgrm. This concentration is so feeble that it makes a direct bactericidal effect very improbable. Moreover I found, as the result of some investigation made in collaboration with Dr. A. Kissmeyer, that a colony of spirochaetes grew well in horse-serum containing 5-10 mgrm. HgCl_2 per litre and still distinctly in serum containing 20 mgrm. per litre. Under these circumstances the aim of the treatment must be to avoid all intoxications in order to avoid damage to the body and its bactericidal forces, but at the same time to maintain a sufficiently high permanent concentration of mercury in the organism without risking an intoxication.

One has to remember that during administration the slow elimination allows an increasing accumulation of mercury in the body. But under a regular moderate supply the elimination can after a time reach an amount sufficient to establish a balance of absorption and elimination, a balance which, if sufficiently high, is eminently suitable for combating the disease. In order to obtain the required saturation of the body more quickly it is of advantage to make the supply of mercury somewhat larger at the beginning of the cure than afterwards.

As to the question of the daily amount of mercury which can be considered sufficient to cover the daily consumption (saturation + elimination), this amount can probably be estimated at 6-10 mgrm. per day according to the size and tolerance of the patient.

Therefore the aim must be to find just such methods of treatment as will provide a sufficient and regular supply to the organism.

The curves of elimination of the different methods of mercury treatment show that this can be obtained by inunctions, by small, numerous injections of soluble compounds and by injections of calomel.

Hydrargyrum salicylicum does not seem to me absolutely reliable, on the one hand because its chemical composition makes it decomposable only with difficulty, and on the other hand because of its extremely rapid elimination. The very common use of this remedy is probably due to the slight painfulness of the injections, but this advantage only justifies its use for exceptionally sensitive patients.

Metallic mercury possesses the same advantage in a higher degree. But this remedy has a very serious drawback in its slow and sometimes very irregular absorption, which may in some cases produce severe intoxication, in other cases a feeble therapeutic effect.

The treatment by *inunctions* possesses the advantage of being reliable, effective and painless, but unfortunately also dirty and tiresome for the patients. To obtain a rapid saturation of the body by mercury it may be of advantage to give at the beginning of the treatment an injection of a soluble salt of mercury, which is rapidly absorbed, or simply to give a dose of 0.5 gram calomel *per os*. This produces the same effect. The daily dose of ointment to be used varies from 3 to 5 grm. according to the size, etc., of the patient. Children support well a comparatively large dose of this remedy.

The treatment by injections of *soluble compounds* is not used very much nowadays, as the injections ought to be given with very frequent intervals (every day, or at least every second day). This makes the treatment rather complicated and wastes the patient's time. This treatment has a special indication in those cases of idiosyncrasia mercurialis, in which a tendency to "hydrargyria cutanea" prevents the use of inunctions.

The treatment by injections of *calomel* has always been estimated to be of great therapeutic value. Still, the painfulness of the injections frequently met with prevents an extensive use of this very valuable remedy. The usual treatment by weekly injections of 8–10 cgrm. often causes considerable pain, but where the same dose is given in two injections every week and in an emulsion of 20 per cent., in my experience this treatment is supported well by most patients. In most cases 3–4 cgrm. per injection will do well and produce a valuable therapeutic effect. The best localisation for the injections is, in my experience, an area a little below the iliac crest and rather to the side. To avoid intravenous injection of the emulsion it is advisable to wait a few moments after the insertion of the needle before the emulsion is injected. If blood exudes from the needle the injection should be made in another place.

BIBLIOGRAPHY.

BÜRGI.—"Grösse und Verlauf der Quecksilberausscheidung durch die Nieren," *Arch. f. Derm. u. Syph.*, 1906.

LOMHOLT AND CHRISTIANSEN.—“Méthode pour doser de petites quantités de mercure, présentes dans les matières organiques,” *Comptes rendus des travaux du Laboratoire de Carlsberg*, x, 1913.

LOMHOLT AND CHRISTIANSEN.—“Bestimmung kleiner Menzen von Quecksilber in organischer Substanz,” *Biochemische Zeitschr.*, lxxxi, 1917.

LOMHOLT.—“Die Zirkulation des Quecksilbers,” *Arch. f. Derm. u. Syph.*, cxxvi, 1918.

LOMHOLT.—*Kvægsolvets Cirkulation i Organismen*, Copenhagen, 1916. (In this a numerous bibliography has been given.)

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.