

A T H E S I S

on

"Schistosomiasis in South Africa".

A Review of the History,

Intermediate Hosts,

Incidence, Signs and Symptoms and Treatment,

based on an analysis of

thirty-four cases.

With an Appendix on

the Recently Introduced Organic Antimony Compounds.

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INTRODUCTION.

"Rooiwater", (Redwater) to the average Afrikander, has been a condition accepted as one of minor encumbrances incidental on his birth in that country. Just like drought and the heat from the torrid sun are unavoidable, so also is "Rooiwater." The loss of a little blood in the urine was of no account - perhaps even a manly attribute - and treatment by a doctor for such a trifle quite preposterous.

This attitude, however, is gradually giving way. Slowly it is being realised by medical men that schistosoma infection resulting in redwater is no longer the harmless condition it was considered. Gradually it is dawning on the profession in South Africa that many vague indefinite symptoms are the result of this infection. Backwardness at school, vague abdominal pains, slight degrees of anaemia are now being recognised as being the direct result of bilharzia. This enlightenment together with the fact that Schistosomiasis is now curable is rapidly leading to a marked alteration in the prevailing conditions. Still perhaps not quite as rapidly as it should. There is still plenty of room for improvement and what is so lamentable is that there are many in the profession however who do not realise this. Many there are

who do not realise the true significance of bilharzia in South Africa, many who have no real understanding of the aetiology and many who are not conversant with the good results of modern methods of treatment.

Schistosomiasis as it appears in South Africa has certain features and peculiarities differentiating it from the type seen in other lands. There appears to be no coordinated account in the literature of Schistosomiasis in South Africa and an attempt is here made to review the position, using the analysis of thirty-four cases personally treated as a background. The observations made on these thirty-four cases are compared with those of other investigators in South Africa and with the findings in other countries.

A brief account is given of

- (a) the history of Schistosomiasis, with special reference to the part played by South Africa in the elucidation of the aetiology;
- (b) the identification of the intermediate hosts and the determination of the species of the molluscs responsible for the transmission in South Africa;
- (c) the incidence of the disease in South Africa with relation to age, sex, race and religion, class of person infected, geographical distribution and the type of schistosome found;

- (d) the signs and symptoms;
- (e) the treatment with special reference to the treatment of the thirty-four cases and a discussion on some of the faults that have marred the progress of the eradication of the disease in the Union;
- (f) the methods adopted in South Africa for the prevention of the disease.

Although in parts there seems to be some adverse comment upon the handling of the position by the Authorities, it has been done in a spirit of constructive criticism, fully realising the difficulties that have been and are still to be overcome.

Throughout reference has been made to the condition as it affects other countries in the hope that comparisons and contrasts may be of value in the final solution of the problem.

An appendix is added on the use of the more recent complex organic antimony compounds so bringing the subject up to date and also in the hope that the information gathered may be of some value in further consideration of the ultimate conquest of the disease.

THE LIFE CYCLE OF THE PARASITE.
(LEIPER).

<u>HOST</u>	<u>TRANSITION</u>	<u>INTERMEDIATE</u>	<u>HOST</u>	<u>TRANSITION</u>	<u>HOST.</u>
Egg	- miracidium				
		(Sporocyst		Encysted in	
		Sporocyst - Daughter		Mollusc	
		Sporocysts		Crustacean	- Adult
		(Sporocyst - Rediae	- cercariae	Insect	
		Sporocyst - Rediae		Fish	
		(Sporocyst - Rediae -		Free	
		Daughter		(Swimming.)	
		Rediae.			

CHAPTER I.

THE HISTORY OF SCHISTOSOMIASIS.

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THE HISTORY OF SCHISTOSOMIASIS

"Stretch out thine hand upon the waters of Egypt, upon their streams, upon their rivers, upon their ponds and upon their pools of water, that they may become blood." (Exodus, Ch. VII, Verse 19).

Egypt has ten out of its fifteen million people infected with Endemic Haematuria. ¹⁵⁵⁾ The waters of Egypt, the streams, the rivers, the ponds and the pools are sources of infection. Can this Mosaic reference to one of the Ten Plagues - the Plague of Blood - visited on Pharaoh, be taken as an indication of the prevalence of Bilharziasis since time immemorial? Or must the ancient Egyptian papyrus of Ebers ²⁰⁵⁾ bear the first testimony to its antiquity? Positive proof of its presence in the Nile Country as early as 1250-1000 B.C. has been supplied by Sir A. Ruffer ²²²⁾ who in 1910 discovered the helminthic ova, in the kidney of a mummy of the Twentieth Dynasty.

The beginning of the XIX century started a flood of literature which was to give much stimulus

to the elucidation of this great problem and scourge. During the invasion of Egypt by the French in 1709-1801 their troops, as mentioned in Larrey's Memoirs,¹⁶⁰⁾ were considerably affected. Later, in 1808, Renault²¹⁸⁾ referred to the peculiar endemic haematuria of the Nile Valley, and 39 years later Pruner²¹⁷⁾ similarly recorded "a peculiar haematuria in Egypt." In the same year - 1847 - Y. Fujii¹¹⁶⁾ referred to an endemic disease in Japan (which was proved later by Katsurada (1904)¹⁴⁹⁾ to be due to *S. japonica*).

It was, however, in 1851 that the first epoch-making discovery took place. Theodor Bilharz, then Assistant Professor in Cairo, in a series of three letters^{23, 24, 25)} to von Siebold - who published them in the following two years - revealed his discovery, of the relationship of a bisexual distome, to the symptoms of haematuria and dysentery, so prevalent in Egypt at that time. To this parasite Bilharz himself gave the name of "*Distome haematobium*," but seven years later Weinland (1858)²⁵³⁾ put Bilharz's *Distome* into a special genus, which he called "*Schistosoma*", and Cobbold⁹²⁾ in describing a similar parasite a little later referred to it under the generic name of "*Bilharzia*".

In 1864 John Harley¹³²⁾ in giving an account of "The Endemic Haematuria of the Cape of Good Hope" to the Medical Chirurgical Society of London, showed that condition to be due to a species of *Bilharzia* which

he called "B. Capensis;" but later in 1871 he admitted ¹³³⁾ that he believed his special species to be identical with that of Bilharz's "Distome," though he found only one form of egg - that with a terminal spine - whereas Bilharz, and also Griesinger ¹²⁷⁾ had described two forms of egg - one with a terminal spine and the other with a side spine. As Harley ¹³³⁾ said: "In all my own cases I can say positively that only one form of egg has existed, viz. that with a terminal spine," and he added, "I have never seen any egg with even a tendency to the formation of a side spine."

In the year, 1870, Cobbold ⁹⁴⁾ began experiments with eggs obtained from patients from South Africa suffering from haematuria, and, although his results gave no clue as to the transmission of the parasite, to him falls the credit of making the first attempt to work out the life cycle. In this he was followed by Sonsino, ²³⁴⁾ Lortet, ¹⁷²⁾ and Vialleton ¹⁷³⁾ and Looss ¹⁶⁸⁾ in Egypt, and a bitter controversy was begun, which was not to be settled until Leiper's ¹⁶⁴⁾ brilliant work in 1915.

To Looss must be given the credit for the minutely fine study of the anatomy of the worm and for redirecting attention to the possibility of skin infection. ^{168, 169, 170)}

Meanwhile, as early as 1893 Sir Patrick Manson ¹⁸⁰⁾ had suggested that there may be two forms of the

disease arising from separate origins. This impression was further strengthened by his discovery ¹⁸¹⁾ in 1902 of lateral-spined eggs only, from a West Indian whose predominant symptoms were rectal rather than vesical, and in 1907 L.W. Sambon ²²⁴⁾ adopted the name "Schistosomum mansoni" for a new species with lateral-spined eggs.

In 1904 Katsurada isolated ¹⁴⁹⁾ from the faeces of patients in Japan suffering from "Katayama Disease" - a peculiar endemic disease characterised by enlarged liver and spleen, cachexia, anaemia and dysentery, and occurring in the district from which it derives its name - eggs, having no spines at all, and to the adults of which he gave the name ¹¹⁷⁾ "Schistosoma japonica." Fujinami, and Nakamura in 1909 established conclusively for Schistosoma japonica the theory of skin infection. The intermediate hosts and stages in the development of the distome were described by Miyairi in 1913, ¹⁹¹⁾ and completed by Leiper and Atkinson ¹⁶³⁾ in 1915, Leiper, ¹⁶⁴⁾ by painstaking researches, worked out also the intermediate hosts and life history of schistosoma haematobium and schistosoma mansoni.

¹⁶⁴⁾ Leiper's work was primarily done with a view to prevention of infection of the huge army of troops concentrated in Egypt, but evidences of the impossibility of the complete application of his findings soon became apparent, for very soon after the

war was over, and even before that time, cases of bilharzia infection began to be reported from all corners of the earth, having been introduced by soldiers returning home from infected areas; to Italy, ¹¹⁹⁾ to Prussia, ²⁰⁹⁾ to Australia ^{110, 239)} and to South Africa. ⁶³⁾

But for Leiper's work this list might have been more formidable. Of the importance of his achievements Sir Patrick Manson in 1917 ¹⁸²⁾ stated: "Dr. Leiper of the London School of Tropical Medicine, by a series of brilliant observations and successful experiments, has now completely filled in the hiatus in our knowledge and has thereby placed in the hands of the sanitarians a sure guide in the developing methods for the prevention of a disease which has hitherto proved the despair of therapeutists."

As the history from this important event onwards is intimately associated with that of the investigations on the intermediate hosts in other countries, and with the introduction of the specific treatment, it will be elaborated further under the appropriate headings.

CHAPTER II.

THE INTERMEDIATE HOSTS OF SCHISTOSOMIASIS.

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The demonstration by Bilharz of the causal parasite naturally stimulated an intensive enquiry into its habits, its spread, its life cycle and its method of infecting man. It was not long before Griesinger ¹⁷⁷⁾ ventured the suggestion that the solution of the spread of Bilharzia "existed in the waters of the Nile, in the fishes which therein abound, or even in bread, grain or fruit"; but Harley in 1864 ¹³³⁾ was the first to point the way, saying: "the ciliated embryo is adapted for an aquatic existence. Swimming freely about, these minute organisms probably come in contact with certain mollusca and become developed within them into what has been called cercaria sacs." Cobbold ⁹³⁾ in the same year, after expressing a similar view - "I think it is more probable that the larva will be found in certain Gastropod molluscs proper to the localities from whence the adult forms had been obtained" - began experiments with a view to tracing the life cycle of the bilharzia parasite through an intermediate host (1870), ⁹⁴⁾ and although unsuccessful, he was the pioneer in this direction. Sonsino ²³⁴⁾ soon afterwards was more fortunate. He tried,

- (1) to infect mollusca experimentally;
- (2) to find species of molluscs

infected with bilharzia larva.

In 1888 Allen ²⁾ at that time the Medical Officer to the Corporation of Pietermaritzburg, writing in The Practitioner, said: "The parasite is practically confined to those who bathe, some streams being more dangerous than others," and commenting on the marked difference in the incidence of the disease among the sexes in the region of the Umzimduzi River in Natal - the boys being heavily infected, whilst the girls are almost free from the disease - he remarked: "not only are the boys more in the habit of bathing than the rest of the community, but they, when bathing, spend much more time in the water." Brock, ³⁰⁾ in 1894 agreed with Allen that "bathing was the most fruitful source of the infection," and continuing this comment, said: "I cannot, among several hundred instances, recall one exception to the rule, that all who suffer from the parasite have been in the habit of bathing." He also added, however, that there is no lack of evidence, "that drinking of impure water is a common factor in the process of infection; indeed it would be unreasonable to think otherwise, if the bathing hypothesis is well grounded. But, other things being equal, the changes of infection occurring will be greater from the large quantity of water which must come in contact with the body in bathing than from the comparatively small amount conveyed into the stomach by drinking."

All, therefore, were in agreement that infection was water-borne, but the same happy state of unanimity did not exist as to the actual stage in the life cycle of the parasite at which it infected men. Was it the miracidia that had hatched out of the egg, or was it a stage which had developed by the passage of the parasitic larva through another host? Sir Patrick Manson in 1905 (Lane Lectures) put forward the opinion that *Bilharzia* is "another illustration of the conveyance of a disease germ through water and probably by a fresh water intermediary." Looss¹⁷⁰⁾ however was strongly of opinion that there was no intermediary; that the egg passed by infected man into water, developed into miracidia which infected man directly. He vehemently denounced all other views, casually dismissing the failures of Wolff²⁵⁴⁾ in German East Africa, Bour in Mauritius²⁸⁾ and Conor in Tunis,⁹⁷⁾ to infect animals with miracidia experimentally, saying that man alone is the host for *Schistosoma haematobia*. Even in 1913, when Miyaira¹⁹¹⁾ after failing with miracidia, succeeded in infecting cats, dogs and cattle with cercaria. Looss, still clinging to his earlier pronounced views, said:¹⁷¹⁾ "Ist dies richtig, dan musste sich *Bilharzia japonica* in ihrer Entwicklung wesentlich von *Bilharzia haematobia* unterscheiden." (If this is true then the development of *Bilharzia japonica* must differ essentially from that of *Bilharzia haematobia*).

Sir Patrick Manson ¹⁷⁹⁾ already the acknowledged "Father of Tropical Medicine," disagreeing with Looss' assertion, answered him: "I would remark that if *Schistosomum haematobium* does not require the services of an intermediate host, its peculiar geographical limitations are difficult to explain."

In 1913 Miyaira and Suzuki ¹⁹²⁾ in Japan, traced the development of *Schistosoma japonica* in a small annicolid snail. The definite intermediate host, however, was finally and conclusively proved to be the mollusc *Blanfordia nosophora*, by Leiper, ¹⁶³⁾ who, as the first Wandsworth Scholar, went out with Atkinson to the Far East. Later he went to Egypt, there to establish, if possible, the intermediate host of the worm which was causing widespread havoc among the troops, and to advise the preventive measures to be adopted. After many vicissitudes, Leiper published the results of his careful and painstaking work in a series of reports in the journal of the Royal Army Medical Corps. ¹⁶⁴⁾ In these he definitely established in Egypt, at any rate, the mollusca intermediary hosts of the *Bilharzia* worm, summing up: "As transmitter of the parasite of urinary bilharzia in Egypt, *Bullinus fulvifilis* fulfils all requirements as far as distribution is concerned *Bilharzia haematobia cercariae* have been found in the species *Bullinus contortus*, *Bullinus dybowski*, and once in a specimen which was recognised as *Bullinus*

innesi. These species would appear to correspond to the forms named *Physa alexandrina* by earlier workers The more restricted distribution of *Planorbis boissyi* would appear to correspond equally satisfactorily with the less universal occurrence of intestinal bilharziasis due to *Bilharzia mansoni* in Egypt The intermediate host of *Bilharzia bovis* remains to be discovered."

The sincere enthusiasm that greeted Leiper's well merited achievements was unbounded. Sir Patrick Manson ¹⁸²⁾ hailed them as "brilliant observations." In an editorial on "Bilharzia" the Medical Journal of South Africa ¹⁸⁹⁾ "The report will be accepted as a monument of industrious, enlightened and fruitful research and the discoveries it disclosed will, we venture to think, be for ever associated with the name of its distinguished author", and continues: "To South Africans these discoveries are of the greatest interest and leave but little more to do than to identify the water molluscs which are capable of acting as their intermediate hosts".

Subsequent experience, however, has shown that the first dart of enthusiasm rather overshot its mark. The matter was not quite so simple. The mystery of a disease that was rife in the times of the Pharaohs, was a world-old scourge of humanity, and which had baffled the intelligence of civilised man for more than four thousand years, revealed

itself; but equally true it was, that the denouement was not real. To identify the water molluscs which are capable of acting as intermediary hosts was not all. Is it not possible that in Egypt a fresh water mollusc was the only intermediate host and, that in South Africa, the development might take place in a species, or even in a genus of quite a different order? Is it not possible that in South Africa there may be even different species of schistosomes from that in Egypt?

THE IDENTIFICATION OF THE INTERMEDIATE
HOSTS IN S. AFRICA.

The determination of the intermediate hosts in S. Africa was initiated in 1916 by the investigations of J.G. Becker ¹⁵⁾ of the Medical Research Institution in Johannesburg, who on the advice of Dr. Watkin-Pitchford, collected twentythree specimens of the mollusc *Physopsis africana* and twenty-three of the species *Lymnaea* from a bathing pool in Nylstroom, which was known to be the source of infection for children who had bathed there. Of the *Physopsis* three were found infected, but of the *Lymnaea* none. Six months later he ¹⁶⁾ was able to identify three male adult worms from the portal vein of a guinea pig which he had injected with cercariae from these infected snails. In the meantime Cawston ^{38,39)} reported that he found *Bilharzia cercariae* in thirteen out of ninety-two specimens of *Physopsis africana* from the Tollgate brickfield in Durban, and the Umzinduzi River in Pietermaritzburg. In a report on the examination of 1,000 molluscs, Cawston ³⁶⁾ states that he found cercariae in *Isidora forskali*, *Isidora tropica*, *Physopsis africana*, *Ancylinae*, *Physopsis Leucheilus*, *Planorbis pfeifferi* and *Lymnaea natalensis*. It is obvious, however, that he was experiencing difficulty in deciding which cercaria belonged to the "*Bilharzia* group", and one may note

too - as will be seen later - the confusion in the nomenclature used, for the snails found. He states that "until the cercariae are fully developed it is impossible to differentiate the distinctly human from the common forms of cercaria with bifid tails."

He quotes ⁴⁰⁾ that in 1910, Dr. J.D.F. Gilchrist, Professor of Zoology at Capetown University, found cercariae with bifid tails in *Physa tropica* (*Bullinus tropica*) and that, that noted authority had difficulty in determining whether the cercariae were of the "human" form of worm.

In 1920 Dr. Annie Porter ²¹¹⁾ incriminated *Lymnaea natalensis* also as harbouring *S. haematobia*, and very soon afterwards ²¹²⁾ reported the presence of cercariae of *S. mansoni* in two out of 1,050 specimens of *Physopsis africana* and in a specimen of *Planorbis pfeifferi* obtained from pools in Mayville, Natal. Becker's discovery, with its definite proof, is a landmark in the history in South Africa, but Porter's identification of the *S. mansoni* cercariae, the adult of which gives lateral spined ova, must not be overlooked: a landmark too, it is, but one, as will be seen later, full of grave forebodings, to South Africa, a country which has since the earliest times of Harley been regarded as the home of the terminal spined egg in its true form.

The entry of another schistosoma into the history is marked by the finding by Cawston in 1921 ⁵³⁾

of ova of *Schistosoma bovis* in the urine of a man, who was passing ova of *S. haematobia*, and also of the larva of *Schistoma bovis* in *Physopsis africana*. The former fact seems to have awakened very little comment at the time.

In 1921 also the ova of *S. mansoni* were reported by the same author to have been recovered from the dejects of a boy bathing in pools at Sydenham, Natal. ^{51,52)}

In 1925 Porter, ²¹³⁾ recapitulating the subject, mentions that apart from the cercaria of *S. haematobium*, *Physopsis africana* harbours twenty-two others species of larva, and, at the same time, she implicates *Physopsis conicum* as a transmitter of *S. haematobia*. To add further to the complexity of the subject Cawston ⁵⁹⁾ in the same year recorded the case of a schoolboy in Zululand who was passing eggs resembling those of *S. bovis*, which he tentatively grouped as belonging to the *Schistosoma spindalis*, Montgomery.

If, as it were, a verification of the presence of *Schistosoma spindalis* in South Africa was necessary, Porter in 1926 ²¹⁴⁾ gives an account of two cases, a European and a native, infected with *S. spindalis*; owing to slight differences in the ova recovered in these cases to those of *S. spindalis* found in Indian cattle, she more precisely named it *Schistoma spindalis* var. *africana*. It is interesting to note, that both these cases had been tending cattle and

goats; that Porter states she was able to infect experimentally *Planorbis pfeifferi* and *Isidora tropica*. These experiments Bequaert ¹⁷⁾ however regards as inconclusive. Cawston in 1926, referring presumably to the same parasite, terms it merely *S. spindalis*.

In 1929, a new species of *Schistosoma* was described by Veglia and Le Roux ¹⁶⁶⁾ who recovered it from some sheep which had died at Humansdorp in the Eastern Province of the Cape. This species they called *S. mattheei* (after the farmer, who first drew the attention of the sheep inspector to the presence of peculiar white lumps in the veins of the dead sheep. As there were no cases of bilharzia in Humansdorp, nor was Le Roux able to find ova in the urine and faeces of native boys, who had been employed in clearing the pond, in which the sheep had been wading, he concluded that *S. mattheei* did not affect man. Curiously enough, these boys had at the time complained of a burning of the skin, and after two hours work in the water were "continually scratching the more tender parts of their bodies." At a plenary session of the Medical Association of South Africa held at Durban in July 1930, Dr. Annie Porter ²¹⁵⁾ says "*S. bovis* - or perhaps a variety only, described by Veglia and Le Roux as *S. mattheei* - has been bred in my laboratory from cercariae found in *Physopsis africana*." She now called the schistosoma, *Schistosoma mattheei-vel-bovis*.

In 1930, South Africa, so as not to be outdone in its hospitality to the *Schistoma* genus, is revealed by Dr. Annie Porter ²¹⁵⁾ as being able to add the *S. japonica* to its already fully stocked list.

"*S. japonicum*, however," she says, "is not endemic in South Africa, and the occurrence of the cercariae (in *Lymnaea natalensis*) may be due to contact of the snail with water contaminated by human excrement from some persons of Eastern origin, ashore temporarily from a ship, the infected snail having been obtained from the Umgeni River near Durban."

Thus it will be seen, as tabulated, the molluscan intermediary hosts for schistosomes pathogenic to man in South Africa, as far as our present knowledge goes, are for *S. haematobia*:- *Physopsis africana*, *Lymnaea natalensis*, and *Physopsis conicum*; for *S. mansoni*:- *Physopsis africana*, *Planorbis pfeifferi* and *Bullinus tropicus*; for *S. japonica*:- *Lymnaea natalensis*; for *S. spindalis* var *africana*:- *Planorbis pfeifferi* and *Bullinus tropicus*; for *S. mattheei-vel-bovis* (as Porter calls it), *Physopsis africana*.

In Egypt ¹⁶⁴⁾ it seems *Bullinus controtus*, *Bullinus dybowskii* and *Bullinus innesi* are the hosts for *S. haematobia* and *Planorbis boissyi* for *S. mansoni*.

"HUMAN" SCHISTOSOMES IN MOLLUSCS IN SOUTH AFRICA.

S. haematobia	S. mansoni	S. japonica	S. spindalis var africana	S. bovis (vel Mattheei)
Physopsis africana.	Physopsis africana.	Lymnaea natalensis	Planorbis pfeifferi	Physopsis africana
Lymnaea natalensis (rare)	Planorbis pfeifferi		Bulinus tropica (Isidora tropica)	
Physopsis conicum	Bulinus tropica			

MOLLUSCS HARBOURING "HUMAN" SCHISTOSOMES IN S. AFRICA.

Physopsis africana.	Lymnaea natalensis	Planorbis pfeifferi	Physopsis conicum	Bulinus tropica (Isidora tropica).
S. haematobia	S. haematobia	S. mansoni	S. haematobia	S. spindalis var africana
S. mansoni	S. japonica	S. spindalis var africana		S. mansoni
S. bovis (vel mattheei)				

No such specificity of host for parasite exists in South Africa, indeed *Physopsis africana*, as can be seen from the table, is quite often infected with other cercariae. Cawston³⁶⁾ in 1916 found 17.4% of a collection from Natal to be infected with *bilharzia cercarcae*; on another occasion two out of seven⁴³⁾ and on a third 15%.⁴¹⁾ Becker¹⁵⁾ found that of thirteen *Physopsis africana* three harboured the parasite while of the *Lymnaea* "not a single individual was infected."¹⁶⁶⁾ Le Roux says "judging from the prevalence of this snail (*Lymnaea natalensis*) throughout a large area of the Union and the localisation of *S. haematobium* only in areas inhabited by *Physopsis*, it would appear that *Lymnaea natalensis* need not be considered as a vector in the spread of schistosomiasis," and Cawston⁶¹⁾ records that he was unable to infect *Lymnaea natalensis* experimentally with *S. haematobia*.

Of *Physopsis conicum* in South Africa, as a host, only Porter makes mention. Thus it will be seen that in South Africa *Physopsis africana* is the main intermediary host of schistosomiasis.

For other countries various molluscan hosts

L. ...	L. ...	
L. ...		L. ...
L. ...	L. ...	L. ...
L. ...		L. ...
L. ...	L. ...	L. ...
L. ...	L. ...	L. ...
L. ...	L. ...	L. ...
L. ...	L. ...	L. ...
L. ...	L. ...	L. ...
L. ...	L. ...	L. ...
L. ...	L. ...	L. ...
L. ...	L. ...	L. ...
L. ...	L. ...	L. ...
L. ...	L. ...	L. ...
L. ...	L. ...	L. ...
L. ...	L. ...	L. ...

TABLE III.

MOLLUSCAN HOSTS OF HUMAN SCHISTOSOMES.

	<u>S. Haematobia</u>	<u>S. Mansoni</u>
Brazil		P.centimetralis P.olivaceus
Cyprus	B.Contortus	
Dutch Guinea		P. olivaceus
Egypt	Bulinus contortus; bulinus dysbowski; Bulinus innesi.	P. boissyi
Gold Coast	Physopsis globosa	
Lourenco Marques	Physopsis africana var globosa	
Madagascar		Planorbis mada- gascarensis
Nyasaland	Physopsis africana var globosa	
Portugal	Planorbis dufourii	
Porto Rico		P.guadelupensis
Sierra Leone	P. africana var africana	
S. Africa	P. africana; Lymnaea natal- ensis; Physopsis conicum	Physopsis africana Bulinus tropicus; Planorbis pfeifferi
Tanganyika	Physopsis nasutu v. martens.	
Venezuela		Planorbis guadelupensis.
W. Indies		P.antiguensis

have been recorded, as seen in table III. For Brazil, *Physopsis centimetialis* and *Physopsis olivacens* by Lutz in 1919; ¹⁷⁵⁾ in Cyprus, *B. contortus* in 1918 by Leiper; ¹⁶⁵⁾ in Madagascar, ¹³⁷⁾ *Planorbis madagascaniensis* by Hasle in 1918; and in Venezuela in 1917 by Itarbe and Gonzalez ¹⁴⁷⁾ as *Planorbis guadelupensis*.

Only in South Africa is *Physopsis africana* a common intermediary host, and in this respect therefore, the Union has its own peculiar problems. It is interesting to note that a variety of *Physopsis africana* - *Physopsis africana* var *globosa* - occurs in infected states in Lourence Marques, Nyasaland and the Gold Coast, and that from the former two countries large numbers of natives are recruited annually for work on the gold mines, though it must be admitted there appears to be no obvious connection between the two facts.

It will not be amiss, to quote here, from Baylis with reference to the naming of the snails. That authority ¹⁴⁾ points out the correct spelling of "Bullinus" is B U L I N U S ; that *Isidora* falls into synonymy with it; and that *Physopsis africana* is a species of the genus *Physopsis*. Le Roux,

| vide p. 8

too, ¹⁶⁰⁾ mentions that "generic names of African molluscs such as *Bulinus* and *Lymnaea* are often misspelt as *Bullinus* and *Limnaia*," and ends by saying that the classification of "the fresh water molluscs of South Africa need revision badly"!

The identification of fresh water molluscs and the various types of cercariae that inhabit them, is a subject bristling with difficulty, and the literature on this matter in South Africa is very confusing. For a private individual, a systematic survey of the snail population of the Union is obviously not conceivable. Such a move must come from authorities with ample means at their disposal, and it is to be regretted that up to the present time no such investigation has been undertaken.

To quote again from the editorial in 1916 : ¹⁸⁹⁾
 "Strange as it may seem, there has been as yet no systematic enquiry into the distribution of the bilharzial disease throughout South Africa," and stranger still, one may add, no systematic survey has up to the present been made of the fresh-water snail inhabitants. ¹⁶⁶⁾ Le Roux, referring to the knowledge in South Africa of the intermediary host,

says: "I would like to point out that the distribution of Molluscs in the Union is imperfectly known and that our field colleagues can supply much of the information wanted." This, in 1929, from the Government Veterinary Research Institute itself! And as late as December 1931 Baylis,¹⁴⁾ of the British Museum, complains that "Great confusion prevails in medicine, veterinary and helminthological literature, in the names used for those hosts. The names in current use are frequently not in accordance with international rules of zoological nomenclature." A study of the South African literature only too readily bears out these words.

Two further factors which present difficulty must be mentioned. Firstly the actual identification of the snail itself is very open to fault and secondly, it is notoriously difficult to assess the type, form and species of the cercariae that are harboured by the snail. In illustration of the first point, it is interesting to note that in 1930 Maass and Vogel¹⁸⁵⁾ from the West Coast, considered it necessary to send the snails they collected to Hamburg for identification, and F.G. Cawston, the most prolific writer on the subject of bilharzia and its intermediate host in South Africa, finds it necessary³⁶⁾ to seek corroboration for his judgment from Burnup of Maritzburg, Dr. Annie Porter of Johannesburg, and even Leiper⁴⁷⁾ in London, and not infrequently with

good cause. That such an experience malacologist can flounder indicates the difficulties, and points to the necessity for such investigation as bilharzia research being tackled by team work; and who can better mobilise, organise and equip such co-ordinated expert undertaking as the central authority, the Government, with all its national resources behind it?

In one respect South Africa is singularly fortunate. In a country so scattered, with less than two million inhabitants, it is a matter of justifiable pride that there exists at Onderstepoort, Pretoria, an Institute of Veterinary Research, and in Johannesburg, less than forty miles away, the South African Institute for Medical Research. The former is wholly controlled by the Government, and the latter partly so. Both institutions have made themselves famous throughout the scientific world, both have produced excellent results in the short period of their existence, and both have proved a source of enlightenment and succour to the revelation of many an obscure scientific puzzle. The work of Sir Spencer Lister, Mavrogordato, and Irving in Johannesburg, Sir Arnold Theiler, De Kock, Le Roux and Quinlan in Pretoria, will stand for all time in the history of successful scientific endeavour. That two, such closely related, institutions should not combine for the joint investigation on this and other subjects strikes one as due to a lack of initiative



FIG. I.

From
 Annual Report of the Director
 of Veterinary Services
 Union of South Africa, 1929.

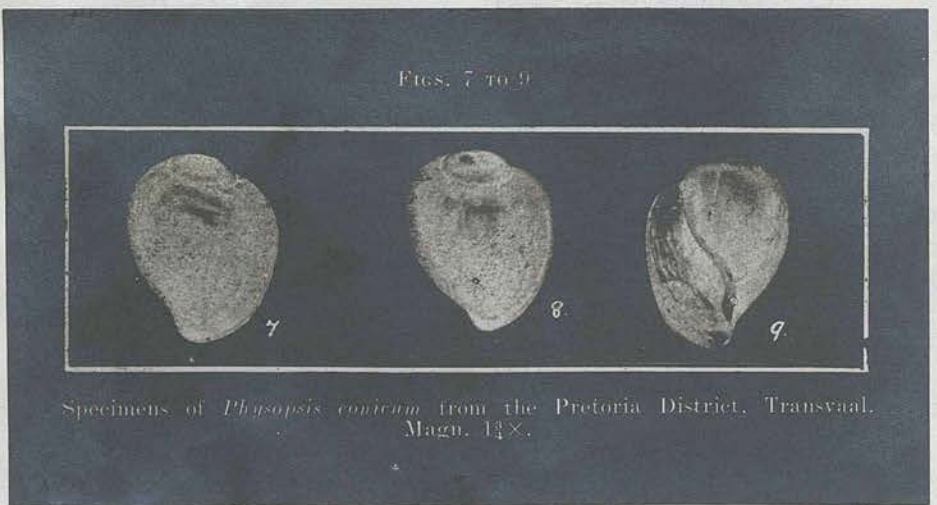
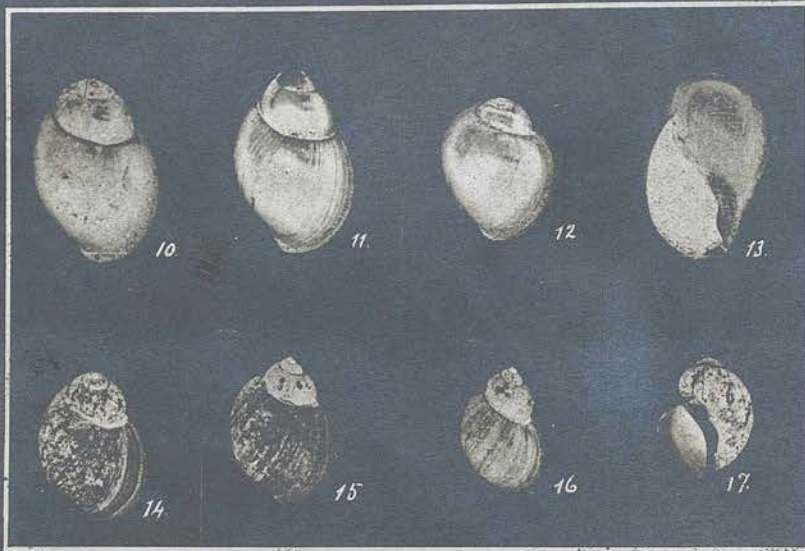


FIG. II.



Figs. 10 to 13.

Specimens of *Physopsis africana* (Krauss) from Natal. Note the difference in the shape of Nos. 10 and 11 and Nos. 12 and 13. Magn. $1\frac{1}{2}\times$.

Figs. 14 to 17.

These are said to be specimens of *Bulinus tropicus* (Krauss). From the Pretoria District, Transvaal. Magn. $1\frac{1}{2}\times$. (See Figs. 32 and 33.)

FIG.III.

From
 Annual Report of the Director of Veterinary
 Services, Union of South Africa, 1929.

on the part of the controlling bodies.

A Brief note on the Bionomics of Physopsis Africana.

Cawston ³⁵⁾ refers to it as "a dark sinistral snail." In South Africa it is found in small pools and overflows of rivers, More particularly in stagnant pools and slowly running rivers, where it attaches itself to the weeds along the banks. They are more numerous in the shallower spruits, streams, lagoons and "pans", particularly favouring those collections of water with decaying vegetable matter on their beds. Most often they are found clinging to the under surface of the blue lotus leaves, on which they feed. ⁶¹⁾ Other favourite food for *Physopsis africana*, according to Cawston, ⁶⁵⁾ is *Nymphaea stellata* and *Cyperus immensus* C.B. Clarke, which are less commonly found at higher altitudes, but occur abundantly in the coastal areas. Curiously enough, for some apparently unexplained reason *Physopsis africana* seem to have a special preference for pools in brickfields. Cawston was puzzled ⁶⁶⁾ as to the problem of the overwintering of the snail, but Porter in 1930 ¹³⁾ showed that *Physopsis* is metamorphosed as sprawn, and *Lymnaea natalensis* and *Planorbis pfeifferi* as extremely small molluscs. Sharp ²²⁸⁾ states that in Natal snails are present all the year round, but are more numerous in the summer months.

T R E A T M E N T.

Case	Sex.	Age	Occupation.	Complaint	Initial Dose.	Maximum single dose.	Total Dosage.	Duration of Treatment	Complication	Remarks	Locality of Infection.	
Johnnie	M	10	Schoolboy	Haematuria ++	$\frac{1}{4}$ gr.	$1\frac{1}{4}$	$18\frac{3}{4}$	29 days .		} Brothers } } Schoolmates }	Skimmerspruit	
Eric	M	8	"	Haematuria +	$\frac{1}{4}$	1	$14\frac{1}{2}$	27			"	
Frobler	M	12	"	Haematuria	$\frac{1}{4}$	$1\frac{1}{4}$	$18\frac{3}{4}$	29			"	
Skinner	M	11	"	Haematuria	$\frac{1}{4}$	$1\frac{1}{4}$	$18\frac{3}{4}$	29			"	
V. de W.	M	9	"	Haematuria +	$\frac{1}{4}$	1	$16\frac{1}{2}$	31			"	
F.F.	M	9	"	Haematuria	$\frac{1}{4}$	1	$16\frac{1}{2}$	31			"	
Johannes	M	10	"	Haematuria	$\frac{1}{4}$	$1\frac{1}{2}$	$18\frac{3}{4}$	29				
Piet	M	27	Gardener	(Asthma Haematuria +	$\frac{1}{2}$	2	$24\frac{3}{4}$	29	(cough, vomiting Herpes Tingling sensation		Also had asthma. (Diagnosed as appendicitis (No haematuria	(Pretoria (West-end.
Venter	M	17	Messenger	Appendicitis	$\frac{1}{2}$	$1\frac{1}{2}$	$19\frac{1}{2}$	25				Daspoort
Baty	M	6	-	Debilitated (Backward at School	$\frac{1}{8}$	$\frac{1}{4}$	12	7 weeks			Debilitated (Backward at school. Tonsils (enlarged.	-
J.L.	M	11	Schoolboy	(Tonsils +	$\frac{1}{4}$	$1\frac{1}{4}$	$18\frac{3}{4}$	29 days			-	
T.P.	M	9	"	Haematuria	$\frac{1}{4}$	1	$15\frac{1}{2}$	29			-	
R.S.M.	M	8	"	Haematuria	$\frac{1}{4}$	1	10	-	Vomiting	Discontinued treatment	-	
Mrs.P.O.	F	34	Housewife	(severe anaemia debility	$\frac{1}{2}$	$1\frac{1}{2}$	$18\frac{3}{4}$	27		(Severe anaemia and debility (Eosinophilia. Ova in faeces	N. Transvaal.	
Muller	M	15	Schoolboy	Haematuria	$\frac{1}{4}$	$1\frac{1}{2}$	21	27			-	
v.Tonder	M	8	"	Haematuria + (Debility	$\frac{1}{4}$	1	$14\frac{1}{2}$	27			-	
Ryan	M	7	"	(Haematuria	$\frac{1}{8}$	$\frac{3}{4}$	$14\frac{3}{8}$	41		Debilitated	-	
MacM.	M	24	Civil Servant	Appendicitis (Backward at School	$\frac{1}{2}$	2	21	19		Diagnosed at operation	-	
L.B.	M	10	Schoolboy	(Haematuria	$\frac{1}{4}$	$1\frac{1}{4}$	15	-		Discontinued treatment	-	
Levy	M	9	"	Haematuria (Backward at School	$\frac{1}{4}$	1	8	-		Discontinued treatment	-	
B.M.	M	14	"	(Debility	$\frac{1}{4}$	$1\frac{1}{2}$	$18\frac{3}{4}$	25	Vomiting	Backward at school	-	
Harris	M	8	"	(Haematuria	$\frac{1}{4}$	1	$16\frac{1}{2}$	31			Scheerpoort	
M.R.	M	10	"	Haematuria	$\frac{1}{4}$	$1\frac{1}{4}$	$18\frac{3}{4}$	29			Nylstroom	
J.H.B.	M	9	"	Haematuria (Tonsils +	$\frac{1}{4}$	1	$15\frac{1}{2}$	29			-	
Richards	M	8	"	(Haematuria Debility	$\frac{1}{4}$	1	$15\frac{1}{2}$	29		Initial complaint, sore throat.	-	
Moon	M	8	"	(Haematuria	$\frac{1}{4}$	1	$15\frac{1}{2}$	29		Debilitated	-	
R.S.	M	9	"	Haematuria	$\frac{1}{4}$	1	15	29			-	
Ted	M	10	Schoolboy	(Anaemia Haematuria	$\frac{1}{4}$	$1\frac{1}{4}$	$16\frac{1}{4}$	25		Anaemic	-	
George M.	M	10	"	Haematuria	$\frac{1}{4}$	$1\frac{1}{4}$	$16\frac{1}{4}$	25			Durban	
A.R.	M	12	Page	Haematuria	$\frac{1}{4}$	$1\frac{1}{4}$	$18\frac{3}{4}$	29			-	
R.L.R.	M	9	Schoolboy	(Tonsils + Haematuria	$\frac{1}{4}$	1	$16\frac{1}{2}$	31		Complaint of nasal obstruction	-	
Henson	M	8	"	Haematuria	$\frac{1}{4}$	1	$14\frac{1}{2}$	27			-	
J.F.	M	8	"	Haematuria +	$\frac{1}{4}$	1	$16\frac{1}{2}$	31			-	
Barris	M	11	"	(Mentally retarded Haematuria	$\frac{1}{4}$	$1\frac{1}{4}$	$18\frac{3}{4}$	29		Backward at school	-	

CHAPTER III.

THE INCIDENCE OF SCHISTOSOMIASIS IN S. AFRICA

although it has been known and repeatedly stated from the earliest times that Schistosoma was a frequent and serious throughout South Africa, no accurate attempt has been made to estimate its extent or prevalence. The various estimates are all based upon the complexity of the problem. Even in certain areas, where the prevalence is so high that the evidence of the disease is obvious to the casual observer, the prevalence of many of the symptoms, and to the disease is often overlooked. Still even in such cases, the prevalence is often estimated upon the probability of identification with the parasite. It might well be that certain cases, presenting signs suggestive of diagnosis of severe ascites, cystitis, renal calculus, dysentery, appendicitis and various forms of dermatitis, if correctly diagnosed could have been revealed as falling under the category of incidence of Schistosomiasis. Thus, in describing his experience on board the S.S. "Palmer", when confined with various peculiar cases, "in which symptoms suggested various forms of disease, such as cystitis, urticaria and dermatitis, he described the condition as 'Schistosomiasis' and 'epidemic', stating that he was afflicted

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CHAPTER III.THE INCIDENCE OF SCHISTOSOMIASIS IN S. AFRICA

Although it has been known and repeatedly stated from the earliest times that Bilharzia was a prevalent disease throughout South Africa, no accurate attempt has been made to determine its exact incidence. This serious omission is in part explained by the complexity of the problem. Even in endemic areas, where the practitioner is on the look-out for evidence of the disease, owing to its insidious character, to the mildness of many of its symptoms, and to the absence of constitutional disturbances, the disease is often overlooked. Still more so must this occur in localities where the practitioner is unfamiliar with the condition. It might well be that doubtful cases, presenting signs suggesting a diagnosis of severe anaemia, cystitis, renal calculus, dysentery, appendicitis and various forms of dermatitis, if correctly diagnosed would have been revealed as falling under the records of incidence of Schistosomiasis. Mann, ¹⁸⁴⁾ in describing his experiences on board the U.S.S. "Helena", when confronted with 14 peculiar cases, "in which symptoms developed varying from acute bronchitis, urticaria and dermatitis, to dementia praecox, associated with Jacksonian epilepsy and hemiplegia", states that he was baffled

until after two weeks of study of the literature and of continued laboratory examination, he was convinced that his cases "with tentative diagnoses of cerebral syphilis, sunstroke, hepatic abscess, etc." were due to bilharziasis. In the scattered settlements of South Africa such facilities for research do not exist.

Another case of difficulty is the failure of many cases to seek treatment. The stoical indifference of the "poor white",* the ignorant labourer and the Boer farmer is amazing. Although the presence of bilharzia infection in the pools and ponds has been known to their families for generations, although they are aware that the natives in their employ have been infected by bathing in certain streams, they still persist in bathing there themselves. The significance of the seriousness of "rooiwater" means nothing to them, and in their judgments the condition is not worthy of necessitating treatment by a doctor. To their mind such symptoms as backwardness at school, anaemia, or abdominal pains cannot possibly be due to

* "Poor White" - The term applied in S. Africa to the lowest social strata of the Europeans. Usually unskilled labourers. "Men, who in a country of blacks, have fallen below the minimum amount of dignity demanded of a white skin." (Sarah Gertrude Millin). They constitute 1/10th of white population of the Union.

Bilharzia. "Rooi water is niks nie", (red water is nothing) says the Boer.

Apart from their parents' indifference, many cases among young boys are not seen, again causing a false impression to be made of the prevalence of bilharziasis, especially as the major incidence is among young boys. The main symptoms - haematuria - being referable to the genito-urinary tract, youths will often out of a sense of sexual shyness hide their state, or if older, and realising the cause, will often be loath to mention the symptom, lest they be reprimanded and punished, for bathing in the streams.

The vast hordes of natives in the Union, of whose numbers no accurate account can be obtained, even for census purposes, let alone for the study of the incidence of disease, is a source of very great error. Only on the mines are they subjected to any semblance of a routine medical examination as a mass. Of the others Dr. Kay Sharp ²²⁸⁾ says: "In Natal it is practically certain that a large proportion of infected natives never come under European medical supervision, there being many tens of thousands of natives who believe implicitly in their witch doctors," and this is true of the rest of the Union. The enormity of the problem can be more readily appreciated when it is realised that in the Union there are estimated to be three natives for each white man, ¹¹⁾ and that out of the 5 million odd

Bantus, these working on the mines only number
 184,000. ¹³⁹⁾

Over and above all these factors, there is the added difficulty that Bilharzia disease is not notifiable. This failure on the part of the authorities in dealing with a communicable disease is a matter of regret, and will be discussed further when dealing with measures for its prevention, and the outlook in South Africa.

Incidence with regard to Age.

In the series of cases under review the youngest was 6 years old, and the oldest was 34. Of the 34 cases 25 were between the ages of 8 and 12 years; 4 occurred in those 12-16 years old; and one each in the age periods 16-20 and 20-25; while 2 were over 25 years old: i.e.

Under 8 years	1 case	2.9%
8 up to 12 years	25 cases	73.5%
12 up to 16 "	4 cases	11.8%
16 up to 20 "	1 case	2.9%
20 up to 25 "	1 case	2.9%
over 25	2 cases	5.9%

The majority of these cases, 85%, were between the ages of 8 and 16 years, i.e. of school age.

Dr. Sharp ²²⁸⁾ the Medical Inspector of Schools for Natal, says: "Approximately 150 cases of schistosomiasis are attending schools in Durban at the present time. This number must necessarily be incomplete, as many may be infected and be unaware of

the fact, and many falaciously regard themselves as cured because the haematuria is no longer evident, and many would not report. However, with a male school population of approximately 5,000 the incidence of this disease, based solely on recorded cases, is 2.4%." At the various "treatment camps" held in S. Africa during the years 1926-1931 under the auspices of the Public Health Department all the cases were school children, viz. 71 from Zeerust in 1926,⁸⁾ and later in the year 27 from the same area. At Rustenburg, in 1927, 66 scholars the ages varying from 8-20 years, and at Zeerust 39; at Nelspruit 50, Louis Trichard 43, 28¹¹⁾ European and 15 native - all children. The Annual Report of the Union of South Africa Health Department, for 1928, states that "thousands of School children in Natal and the Transvaal Province suffer from bilharzia and adds: "There is reason to believe that in many districts of the Transvaal prevalence of the disease has greatly increased during the past few years."

The earlier literature from South Africa shows that the great prevalence among the young is not of recent development. In 1864 Mr. George Dunsterville, surgeon in Port Elizabeth, says (quoted by Harley¹³²⁾): "It (Bilharzia) affects boys at the age of 3-4 years and is most prevalent between this age and 16. Two out of every three schoolboys are affected by it. It gradually disappears about the

age of puberty." Of the 34 cases personally observed only four were above the age of 16 years. Nearly all the numerous cases recorded at various times by Cawston are of school children, and he states ⁵⁸⁾ "in some districts the majority of the school children have suffered at some time or other."

In other countries, too, the main sufferers are those of school age. As early as 1834 Salesse ²²³⁾ mentions that "three quarters of the children of the Isle of France are attacked with haematuria." In Bo, Sierra Leone, at the school for the sons of chiefs, 75 scholars are quoted by Butler ³³⁾ to be infected, without showing signs. Christopherson ⁸⁹⁾ writing of Egypt, points out that bilharzia is essentially a children's disease. Leiper ¹⁶⁴⁾ in 1915 by a rapid examination of the urine of 54 boys in the Marg canal region found the bilharzia eggs in 49. In the French military zone of Guinea, Clapier ⁹⁰⁾ found that bilharziasis occurred in 11 out of 54 children from 5-15 years old, and in the Toma country it occurred in every second child. He also states that in the adult male the incidence lessens towards old age. In the Orphanage at Jaffa 43% of the children between the ages of 9-14 were found by Felix, ¹¹³⁾ to be infected on one occasion and 6.25% on another; and at Togo, Peltier ²⁰⁴⁾ writing in 1925 says that almost all the children 8-10 years of age suffer from parasitic haematuria.

Incidence with regard to Sex.

As will be seen from the section dealing with "age", most of the cases occur among boys. In the group of cases analysed only one was a female, and most references in the literature show a similar distribution among the sexes. Again, referring to Mr. Dunsterville's account ¹³²⁾ in 1864, it is seen that he mentions "the female sex and the native population are free from it."

Although the late Dr. Gibson, ^{121,122)} Honorary Gynaecologist at the Johannesburg Hospital gave a lucid account of bilharzial lesions in the female, there is no doubt that the disease is not common in that sex. In 1930, out of 371 ¹³⁾ post mortems performed by the staff of the South African Institute for Medical Research, who are responsible for the pathological department in the Johannesburg General Hospital, in 13 there were lesions of bilharzia found, and of these only one was in a female.

With few notable exceptions this is the experience universally. These exceptions are outstanding and of considerable interest. Thus Bettencourt, Borges and de Seabra ²¹⁾ record that 46 of the 47 verified cases of bilharzia at Tavira in Portugal were women or young girls who washed clothes in a basin there. The one exception was a boy of 13 who had bathed in the water. The other locality where females particularly are prone to infection is in

Toma, where according to Clapier ¹³³⁾ it becomes increasingly prevalent with old age. This, he explains, is due to the domestic duties of the women, who not only wash calabashes and household articles, but carry water and do fishing while the men work in the fields, which are not irrigated as in Egypt.

Incidence with regard to Race and Religion.

In South Africa race and religion does not seem to be a great factor in the incidence of the disease. That all the cases recorded were Europeans is of no significance. That was merely due to the type of practice in which the opportunity was afforded of studying the cases. In Natal, Sharp ²²⁸⁾ points out that Schistosomiasis is not confined to the European population, but also occurs among the natives and Asiatics. Indeed, Cawston ⁵⁸⁾ states that "in certain parts of the country the natives would appear to be the principal sufferers." The records for 1929 of the South Africa Medical Research Institute show, that, out of 345 post mortems held, 13 cases showed evidence of bilharzial infection, and of these, 8 were natives, 2 were Europeans, and 3 were Eurafricans.

Dr. L.J.J. Orpen, ²⁰³⁾ Additional Health Officer for Southern Rhodesia, in 1916 on examining 592 natives, found that the various tribes were not differentially affected. His figures are:

	<u>No. Examined</u>	<u>Infected</u>	<u>Percentage</u>
Nyassaland	163	36	22.1
Portuguese East Africa	172	65	37.7
Mashonas	176	64	36.4
Zambesis	22	3	36.4
Zulu	4	1	25.0
Basuto	4	1	25.0
Cape Boys	14	3	21.4
Zanzibar	4	1	25.0
Bechuana	2	1	50.0

Thus all the tribes seem to be equally heavily infected. For the Bechuana tribe the figure of 50% obviously cannot be considered reliable, as the number examined was far too small - only two.

Natal, with its polyglot population, numbers a fair percentage of Indians among the inhabitants. That they, are not spared, is evidenced by Sharp's figures. ²²⁸⁾ "In one Indian School at Stanger 40 out of 300 children passed ova in the urine. At the Umgeni Indian School 19 out of 190, and at the Depot Road Indian School 17 out of 480." ⁵⁸⁾ And Cawston who must be regarded as the best authority in Natal on the subject, - says that in some Indian schools over 40% of the children complain of haematuria. That, in India, the infection is so rare, therefore, can be accounted for by the geographical and

biological characteristics of the country, rather than by any immunity existing among its people.

The frequency of cases among natives outside South Africa is legion, West Africa, Nyassaland, Somaliland, the Congos, Liberia, Mauritius, Madagascar, to mention but a few countries, is sufficient to prove the ubiquity of the disease among the "blacks", and to show that the Union is not especially picked out.

From a religious point of view it is difficult to draw comparisons in South Africa. Many of the Indians are no doubt Mohammedan, many of them are Christian, some are Hindu and some are Buddhists, etc. Of the natives, the majority are innocent of any religious conviction, though some profess to be Christians. The white population, with the exception of a fair proportion who are Jews, are all Christians. Of the cases recounted all, were Europeans and therefore, belonged to the Christian Church, with one exception - the boy Levy, who was Jewish.

The question of religious practices and their bearings on the incidence, while of no importance in the Southern part of the African continent, is a more pertinent one in the North. In the Near East there are at the present time living side by side large numbers of Christians, Mohammedans and Jews, under similar conditions of climate and environment

and a comparison of the incidence among them is enlightening. Dr. A.H. Hall, reporting on Bilharzia Disease in Basrah ¹²⁹⁾ shows that half the population of school age are infected, and about a third of the adult working population suffer from it. From the comparative results of the examination of pupils at the American School, he concludes that Christian and Jewish children showed less susceptibility than the Mohammedan children. He found that

among the Mohammedan children	57%
" " Christian	30%
" " Jewish	27%

were infected, and presents the possible explanation that the Christian and Jewish school children bathe much less frequently in the creeks, than do their Mohammedan colleagues. While not presuming to criticise the opinion of an observer more conversant with local customs, attention might here be drawn to the views of Diamantis. ¹⁰⁵⁾ He believes that the difference between the incidence in males and in females is due to the religious ablutions, six or seven times a day imposed on Musselmen, and which are rarely practised by women. Christopherson, too, lays stress on the Koranic Law as a factor in the spread of helminthiasis in Egypt. The difference in the incidence between the Christian and the Jewish school children is so small as to bear little significance, though Cawston ⁵⁰⁾ seemed impressed with

the Talmudic injunction, forbidding the bathing in any collection of standing water or water infested with snails, as responsible for the absence of Bilharzia throughout the centuries in Palestine.

Though the work of Leiper, ¹⁶⁴⁾ Atkinson, ¹⁹²⁾ Miyaira, Suzuki, and others, have left no doubt as to the exact route of infection, it is very interesting here to recount the words of Allen in 1888. ²⁾

"Boys swimming or wading in the water stir up the resting place of the flukes at the bottom. Then the opportunity would be presented for its entry outside the body, first gaining access to the sack-like receptacle formed by the prepuce in boys, from which point it could easily enter the unprotected surface of the urethra. It is very probable that in ancient Egypt the presence of this little fluke in the waters of the Nile suggested the adoption of the operation (circumcision) that the Jews who have faithfully preserved it, adopted the custom and carried it with them when they left Egypt, and that gradually the cause of its origin became forgotten, and it advanced from being a sanitary precaution to a religious rite."

"In other parts of Africa, where the fluke exists, circumcision has been or is practised, at present in our own neighbourhood among the Basutos, and at one time, almost within living memory, amongst the Zulus. If these and other people of the Abantu

race really did migrate to the south, from the Valley of the Nile, or among the hills of N.E. Africa, it is at least likely that it originated as a protection against this fluke. And it will have to be practised again, if the Europeans, or indeed any race, is to maintain its normal vigour in the infested countries."

Incidence with regard to Class.

Under this heading will be considered the social status, the mental level, and the occupation of those exposing themselves, and those already infected.

That practically all the cases under observation were schoolboys is incidental on their youth, and the philosophic outlook (if youth can be credited with design in its actions) belonging thereto. The proclivities and the enthusiasm of young age, in conjunction with the climatic conditions, are such as to present the most favourable set of circumstances for infection. "Boys will be boys", no matter where they live, and fishing in streams and bathing in rivers are their universal practices. More so still is this danger present in a warm climate, where facilities for supervised bathing places are scanty. Only in the towns are there regular swimming baths, while in the rest of the country scattered collections of water in small amounts - not infrequent in localised areas, - have to serve this purpose. As Allen ²⁾ wrote 44 years ago, so is the position today; "but children, more particularly boys, will bathe; in a

hot climate like this the temptation is too great to be resisted, and to deprive them of the pleasure and benefit of swimming would be serious indeed; not that I think it would be a lesser evil than becoming affected by the fluke."

In this connection it is interesting to note that seven of the thirty-four cases recorded, were school-mates from the same school, who presumably spent their leisure hours together, bathing and wading in the spruits, * in the vicinity of their homes. It might be of interest here to mention a theory of Cawston's ⁵⁸⁾ that the practice common among young boys of putting on their shirts after bathing without drying themselves greatly increases the chances of infection, the cercariae becoming attached to the skin while bathing.

The mentality of the "poor white" and their outlook towards the disease, or to anything for that matter, is such as to render them an easy prey to the penalty of their own ignorance and slothfulness. Cleanliness and the elementary principles of sanitation are foreign to them, and as Cawston remarks: ⁶⁵⁾ "the principal source of infection is the bathing pools which are used for paddling, bathing and fishing by indigent persons at brickfields." In numerous

* SPRUIT -----
The S. African term for small stream.

other ways do they form a class, especially liable to infection. Warning notices of the danger of bathing in streams, efforts to dissuade them from foolishly exposing themselves, attempt to inculcate into them the value of hygiene, are wasted on them, like water on the arid soil, they are too lazy to till. They compare in some ways to the class on whom the greatest incidence falls in Egypt - "the fellaheen, the fiki and the Moslem priest," of whom Girges says "their ignorance and poverty prevent them from seeking early advice."¹²³⁾

Among the cases analysed the majority, as stated, were young boys. The mental level and social status as a factor in their cases were of little account, in explaining their contracting the disease. Most of them came from fairly decent homes, their parents being hard-working, respectable middle-class people, and the main cause of their infection being the circumstances recounted above.

The instance of the infected laundresses of Portugal²¹⁾ finds no equivalent in South African literature. In Toma⁹⁰⁾ as pointed out, the women, in virtue of their occupation of fishing and washing goods are also the class more heavily effected.

Troops, since the earliest records of military medicine, have been the means of spread of infectious diseases. Syphilis, gonorrhoea, cerebro-spinal meningitis and typhus, stand out as glaring examples.

Bilharzia is no exception. When it is recalled that it is within the memory of the present generation that masses of troops were concentrated along the banks of the infected streams of South Africa, that during the Boer War 625 men ¹⁰⁰⁾ were infected, the significance of military movements in increasing the incidence of the disease is apparent. Numerous instances of infection of troops occur in the literature of military campaigns. During the Napoleonic wars, during the Boer War, ^{134, 85, 167)} and during the Great War, ^{239, 209, 110, 1, 32)} and even in times of peace. ⁹¹⁾

Incidence with Regard to Geographical Distribution.

Dr. A.J. Orenstein, lecturer on Tropical Medicine at the University of Witwatersrand, in a paper read before the Third Annual Scientific Meeting in 1930, said: ²⁰¹⁾ "The infection is, of course, very widespread in the Union, especially in the rural areas and coastal belt." 66 years previous to this, Mr. Dunsterville had said, ¹³²⁾ "Haematuria is common in Uitenhage and in Port Elizabeth. It has been prevalent in the former town Two out of every three schoolboys are affected by it." Harley himself wrote, ¹³²⁾ "I have ascertained the following facts, viz: (1) that the disease prevails in Natal; (2) that in the Cape Colony it appears to be limited to Port Elizabeth and Uitenhage." In 1864 Dr. J.W. Johnson, Assistant Surgeon to the 85th

Regiment, wrote: ¹³²⁾ "Haematuria prevails to some extent among children of the civil community of Natal", and he records a family of three brothers infected from the Sterk spruit, a tributary of the Umlazi river near Pietermaritzburg. At the same time Mr. George Saunders, ¹³²⁾ staff surgeon, wrote: "While in Port Elizabeth I was greatly struck with the number of cases of haematuria in young boys, and on enquiry was informed that the disease was very common at Uitenhage", and he added, "I have never met with haematuria at Grahamstown, which is 95 miles from Port Elizabeth, nor at Fort Beaufort or Alice, 50 miles up country." And Mr. Robert Speedy ¹³²⁾ of the 45th Regiment added further to this account that "Haematuria was not prevalent either at East London or King William's Town." Thus it seems that it was early recognised and commented on that the infection was localised to certain endemic areas.

In 1929 Le Roux ¹⁶⁶⁾ in the Annual Report of the Director of Veterinary Services for the Union, says, "Schistosomiasis is by no means so widespread, as is suggested by the chart published in Byam and Archibald. That chart is a mis-statement of facts. The disease seems localised to certain well defined areas." While realising, that the distribution of bilharzia in South Africa is at present poorly defined, as is the incidence of the intermediary host,

yet from a perusal of the medical literature of the country, support is given to Le Roux's views. Reports of cases appear to emanate from the same sources repeatedly, and until a systematic authoritative survey and referendum is made, the whole question must be regarded as unsettled. Certainly the probability of such a position obtaining is highly suggestive. Owing to this omission the interests of the subject can be best served by reviewing the geographical distribution of cases recorded.

Although Byam and Archibald in the edition printed in 1923, chart as infected the Transvaal, Orange Free State, Natal and the whole of the Cape Province, the Annual Report of the Union of South Africa Health department for 1925 reads: "Bilharzia infection of various species of fresh water snails is endemic and occurs over a wide area of the Union; a hundred mile wide coastal belt, from Knysna to Lourenco Marques, representing, roughly, the portions of the Cape Province, Natal and Zululand, affected. All the Union North of a line drawn from Lourenco Marques to Lichtenburg and beyond may also be considered as infected, or potentially infected."

That this is the more correct version cannot be doubted. No reference can be found in the literature of cases contracting the disease West of Knysna, though there are instances of treatment being undertaken of cases infected elsewhere. 167, 98)

Sharp, ²²⁸⁾ writing of Natal, says: "The coastal area of the province is heavily infested: practically every river has at some time been infested at its mouth The occurrence of urinary schistosomiasis is favoured by a tropical or semi-tropical climate, slowly moving waters, spruits, lagoons and pans which are a suitable habitat - i.e. with much vegetation - for the intermediary hosts." And Cawston ⁵⁷⁾ in 1924 says that "the infection exists in rivers flowing west just as surely as in those which empty into the Indian Ocean."

From Natal, Cawston records numerous cases. From Sydenham ^{51, 52, 53)} Mayville ^{54, 58)} in and around Durban and Pietermaritzburg, ⁴³⁾ New Hanover ⁶⁵⁾ and was there infected himself. ⁵⁵⁾ All the rivers along the South Coast seem to be affected, and many of them are definitely known to be so. ⁵⁷⁾ viz, the Umzinbi, Umtwalumi, Iffafa, Umzinto, Isezelz, Umpambinyoni, Umlas, Umhlatuzan, and the Umbilo rivers. Higher up in the hills only the Umsinduzi, a tributary of the Umgeni, and the Dorp Spruit, which flows ultimately into the Tugela River, near Maritzburg, are infected.

Of cases contracted in the Orange Free State there is only one reference in the literature, and that of doubtful origin, namely, the case of the soldier quoted by Lillie, ¹⁶⁷⁾ who became ill soon after leaving Bloemfontein.

The Cape Province is much more heavily attacked, but only in its Eastern half. ^{167, 246)} . The

country of the Transkei and Griqualand East particularly so. ²⁴⁶⁾ Port Elizabeth and Uitenhage furnish the earliest cases in the literature. ¹³²⁾ In 1901 ⁹⁸⁾ a correspondent in the British Medical Journal pointed out that in King Williams Town hardly a boy who bathes escapes, and it is interesting to note that in 1916 very few fresh cases were seen in that town, due no doubt to the stopping of river bathing. ³⁷⁾

The Transvaal, however, seems at the present time to be usurping Natal's position of premier in the list of heavily infected provinces. The treatment camps of 1926, 1927, 1928, etc. were all held in the centre of heavily infected areas. Zeerust and Rustenburg in the west, ⁸⁾ Louis Trichard and Nylstroom ^{9, 11)} in the north; and Nelspruit, White River, Ohrigstad, Groot Marico, and Piet Retief in the East. ¹⁰⁾ Other localities in the Province implicated are: Middleburg, by Rousseau and Spencer ²²⁰⁾ and Cawston, Zoutpansberg district in the north, and Magaliesberg ⁶²⁾ towards the south. With regard to some particular places, the words of Cawston are of great significance: ⁶²⁾

"Of special interest is the discovery by me of the snail (*I. africana*) in the Hartebeespoort Dam, where no prophylactic measures have been enforced, to keep down the large number of fresh water snail that were breeding in the shallow portions, of this popular picnic place for Pretoria and Johannesburg

pleasure parties. Previous to this discovery I had myself collected the species, heavily infected with schistosomiasis, from one of the rivers, that feeds the dam and had treated a boy from this neighbourhood who was heavily infected with the bilharzia parasite."

At Mulder's Drift and Magaliesburg ⁴²⁾ where the river runs into the Little Crocodile River the country abounds with infected cases, yet in places like Potohefstroom, not far away, the condition is unknown. ⁴⁴⁾

It is interesting to append the report from the Transvaal Education Department for 1930: "Investigations in Pretoria since August 1930 show that there is practically no safe bathing place within the vicinity of the Pretoria Municipal Area outside the Municipal Swimming Baths. The following waters are decidedly dangerous, West End Golf Course Spruit, Skinner's Spruit, Aapies River, Pienaar's River, river running through Silverton and Derdepoort, Crocodile River below Hartebeestpoort Dam, and at Pelindaba, Swaartspruit, Hennops River and Six-mile Spruit. In fact, North, East and West of Pretoria practically all water must be regarded as probably infected." Almost all these areas are favourite picnicing, fishing and bathing places.

The actual sources of infection in the cases recorded were impossible to determine, except in the cases of the seven schoolmates who bathed at

Skidderspruit and of another five who had been bathing in streams or pools at such places as Daspoort, Pretoria West, Scheerpoort, Nylstroom and in the Northern Transvaal.

Incidence with regard to the types of Schistosomes found in man in South Africa.

I. Schistosoma haematobium.

This is the commonest form, and was present in all cases recorded, both in this series of thirty-four cases and in the South African literature with the exception that

II. Schistosoma mansoni - has been found on the following occasions:

- (i) Cawston in 1921 in Sydenham Natal. ^{51, 52)}
- (ii) Porter 1918 2 cases. ²¹⁰⁾
- (iii) In 1930, ¹³⁾ the report of the South African Institute for Medical Research states that *S. mansoni* was found at post mortem alone on six occasions; with one or more other parasites - such as *Entamoeba histolytica*, *Ancylostoma duodenale*, *Ascaris lumbricoides* and *Schistosoma haematobium* - on eight occasions.
- (iv) In 1930, the same report ¹³⁾ records the finding of *S. mansoni* in the transverse colons of three natives who died within a fortnight at an East Rand gold mine. "Each case was one of typical biharzial dysentery!"

III. Schistosoma bovis, or Schistosoma mattheei-vel-bovis.

- (i) In 1921 Cawston ⁵³⁾ already noted.
- (ii) In 1930 Cawston ⁷¹⁾ says that *S. bovis* has been found in man in Natal, but gives no details - he may be referring to the case in 1921.

IV. Schistosoma spindalis or Schistosoma spindalis-
var-africana.

- (i) In 1925 Cawston ⁵⁹⁾ already noted.
(ii) In 1926, Porter ²¹⁴⁾ two cases already noted.

V. Schistosoma japonica.

1930 By Porter at Durban ²¹⁵⁾ already noted.

The occasional finding in South Africa of Schistosomes other than *S. haematobium* is only of recent occurrence. Since the time of Harley's announcement in 1864 only the one form of egg was found.

It is only since the war that *S. mansoni* has been reported in S. Africa and it seems probable that just as infection was brought from Egypt to other countries, so also was it introduced to S. Africa. ⁵²⁾ Another possible source is the group of natives from Portuguese East Africa recruited for work on the Gold mines. In fact most of the cases recorded were in mine natives. ¹³⁾

With reference to the occurrence of *S. bovis* or *S. mattheei-vel-bovis* (as Porter calls it) it must be pointed out that *Physopsis africana* harbours *S. bovis*; ¹⁶⁶⁾ that Porter considers *S. bovis* identical with *S. mattheei*; and that *S. mattheei* is prevalent among sheep in the Eastern Cape Province. The significance of these facts is patent. Christopher-son suggests ⁸³⁾ that in cases of bilharzia (apparently due to *S. haematobium*) where there is no bladder in-

volvement the condition may be due to *S. bovis*.

Also the finding of *S. spindalis* (-var-africana) opens up grave possibilities of a widespread dissemination of the disease. It is significant that both cases reported by Annie Porter had been working with cattle (the Schistosome having been till then regarded as occurring in cattle only).

The presence of *S. japonicum* in *S. africa* on one isolated occasion can be explained as Annie Porter points out as due to the accidental infection of snails by some person from the East temporarily ashore at Durban.

CHAPTER IV.

THE SIGNS AND SYMPTOMS OF SCHISTOSOMIASIS.

The malaise and lassitude which the majority of the subjects towards "Newly-arrived", and also which cannot be already been seen, is due in part to the very nature of the signs and symptoms in most cases, all they usually occur on South Africa. This malaise developed and became so marked in his psychology that some individuals became in a degree, and the frequency of "Newly-arrived" is due to the fact of his

CHAPTER IV.

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occurrence of anaemia was incidentally discovered in the course of a complete medical examination for the details of different complaints - some on account of very slight, some because of nasal catarrhs, some on lack of appetite as a symptom, and some on account of diarrhoea as a result - and not a few on account of chronic and debility. The majority, however, had no previous, persistent symptoms - anaemia.

Incubation Period.

This is stated by Ryan and Griffiths to be present four to ten weeks after exposure. It is evident that this can only be regarded as a maintenance of the disease occurring in recent arrivals to endemic areas.

CHAPTER IV.THE SIGNS AND SYMPTOMS OF SCHISTOSOMIASIS IN S.AFRICA.

The undisturbed attitude which the Afrikander adopts towards "Rooiwater", and upon which comment has already been made, is due in part to the very mildness of the signs and symptoms in most cases, as they usually occur in South Africa. This nonchalant demeanour has become so rooted in his psychology that even when profuse haematuria is present, and the diagnosis of "Rooiwater" is made by himself or his friends, he still regards the seeking of medical aid for such a "trifling matter" with contempt.

In many of the cases personally recorded the presence of haematuria was incidentally discovered in the course of a complete routine examination for some totally different complaint - some on account of sore throats, some because of nasal obstruction, some for lack of appetite as a symptom, and some on account of backwardness at school, and not a few on account of anaemia and debility. The majority, however, had one prominent, persistent symptom - haematuria.

Incubation Period.

This is stated by Byam and Archibald to be some four to ten weeks after exposure. It is evident that this can only be estimated from instances of the disease occurring in recent arrivals to endemic areas;

the local population having in all probability been infected and re-infected since their youth. Various figures are given by different writers as to the length of the incubation period. Hatch,¹³⁸⁾ in 1887, said one month; Beveridge in 1907¹⁹⁾ found it in seven cases to vary from 12 weeks to six and a half months, the majority being four months; while Abercrombie gives it as from one to two months. In South Africa, Sharp²²⁸⁾ reckons it as from three to six months, and with this Cawston⁵⁸⁾ agrees.

In the cases recorded no estimation whatever could be made of the incubation period. Many of the children had bathed and played in the streams and spruits since the time that they could walk.

Early Signs and Symptoms.

Of recent years a number of observers have pointed out a peculiar sense of tingling and itchiness of the skin experienced by bathers, in infected streams, when they came out of the water. Smith²³⁹⁾ refers to it, as having occurred among some Australian soldiers who had been swimming in a canal at Tel-el-Kebir, Egypt. Cawston⁴⁹⁾ corroborates this observation, and says:⁵⁸⁾ "The earliest symptoms of bilharzia infection are generally overlooked. Persons who bathe in infected water often remark on a tingling sensation of the skin on coming out of the water." In this connection it is interesting to re-



call that the monkey, used in Leiper's experiments showed, by peculiar movements, and by refusing to drink on the following day, that he must have experienced similar unpleasant sensations when he wets his mouth with infected water. Le Roux, in his polemic "Can Schistosoma Mattheei Infect Man?"¹⁶⁶⁾ mentions, that the native boys, sent to clear the dam, where the infected sheep had been drinking, complained of a burning feeling of the skin, after two hours immersion in the water.⁹⁹⁾ Cort and Christensen and Greene⁷⁸⁾ described in 1928 a peculiar type of dermatitis with itchiness of the skin among bathers in Michigan and at Minnesota, respectively, which they state is due to cercaria liberated by the local snails. The cercaria were not of bilharzial origin.

In this respect also it is interesting to note the close relationship between the

- (a) early stage of schistosoma haematobium infection, which is the type prevalent in South Africa;
- (b) the itchiness of the natives, during the investigation of the life cycle of Schistosoma mattheei;
- (c) the "Michigan Dermatitis" and Minnesota "swimmer's itch", and
- (d) the extreme itchiness of the skin termed "Kabure Disease" which is the initial stage of the Katayama Fever due to infection with the Japanese variety of the Schistosoma - S. japonica.

Early signs and symptoms are stated to be due to toxic absorption and are "generalised urticaria with

pyrexia, rigors, abdominal pain, pulmonary symptoms, emaciation, an increased leucocytosis and high eosinophilia" ²²⁸⁾ or, as Cawston says, ⁵⁸⁾ "irregular temperature, biliousness and urticaeia "and in young persons there is also slight digestive disturbance, occasional vomiting, constipation, and giddiness! Sharp, ²²⁸⁾ commenting on the prevalence of these early symptoms in the young, says: "school children in the endemic areas of Natal do not as a rule complain of, or even notice these preliminary complications." By the cases personally observed, no mention was at any time made of symptoms, such as above, and in this respect the findings coincide with Sharp's experience.

Symptoms and Signs of Established Disease.

Haematuria.

The earliest and most obvious sign as a rule is haematuria. Of the seven school mates in the series of cases treated all complained of this symptom. In the first child, to be brought, there was a very severe loss of blood, in two it was moderately severe, and in the remaining four it was slight or intermittent. In all the other cases with three exceptions haematuria was a symptom at some time or other; either voluntarily admitted, or confessed after questioning. The three exceptions will be elaborated later.

Allen's ²⁾ classification of the degrees of severity of the haematuria is very useful:

1. Few drops of blood after micturition.
2. Urine bloody.
3. Blood during micturition and also continuously (rare).

Byam and Archibald describe as the commonest sign "a painless terminal haematuria." This was the type in practically every case investigated. The severity of the haemorrhage varied from being very profuse and continuous, as in the case of "Johnnie" from Skinnerspruit, to a very occasional few drops after micturition just sufficient to stain the shirt. As Mr. Dunsterville said ¹³²⁾ "The shirts of boys affected with the disease are often stained as if they had the menstrual discharge of the other sex." The Haematuria may gradually diminish of its own, but is usually aggravated by exertion or exercise on a hot day, and by travelling. Playing games had a decided influence in this direction on a few of the cases observed.

Though a very common symptom, haematuria is not always present as such. In 1929, Gopsill ¹²⁴⁾ found in the urines of 100 adults admitted to Port Herald Hospital in Nyassaland, and giving no history of haematuria, eggs of schistosoma haematobia. In some of the cases of long duration where the bladder wall has become thickened and covered with papillomatous growths, severe haemorrhage may occur at times.

Pain.

Pain is not a common symptom. Backache is not infrequent in those cases with signs of cystitis, but in severe cases with septic vesical infection - a condition very rare in South Africa ²²⁸⁾ pain on micturition is usual. Transient dull pains in the loins and suprapubic area have been described, but these were not present in any of the cases recounted, nor has Sharp ²²⁸⁾ noticed this symptom in Natal. This, presumably, is due to some degree of cystitis. Renal colic, according to Cawston, is not uncommon in South Africa, though its occurrence in Egypt in cases of bilharzia has frequently led to a wrong diagnosis of calculus. ¹⁴¹⁾ Potts ²¹⁶⁾ records a case of a patient age 14, infected while living in Northern Transvaal, who had pain in the kidneys, most marked when lying down. Whether this was due to renal calculus or hydronephrosis with slight kinking of the ureter is difficult to make out.

Frequency of Micturition.

Pain and frequency of micturition is occasionally seen, the latter more particularly. The pain is of a burning character and is especially noticed towards the end of micturition. It may even precede the appearance of the haematuria. Later the irritation becomes persistent, resulting in frequency of micturition and later still on account of the presence of large clots the symptom is further aggravated.

Though Byam and Archibald say that urgency is a common early symptom, this was not noted in any of the cases.

Mucoid Discharge.

The presence of a yellowish, translucent, mucoid jelly-like substance appearing from the urethra at the end of micturition - and in some cases replacing the blood in the urine after the first few injections of antimony tartrate - is a sign not mentioned in the literature reviewed. So consistent was this sign, so frequent its appearance and, judging from its occurrence as an intermediate stage in the disappearance of the blood, it was regarded as a characteristic sign of a mild infection, and as an index to the progress of treatment.

Backwardness at School.

Of all the signs and symptoms with bilharzia as the causal factor, this perhaps is more often missed than any other. That this is a matter now being clearly recognised can be seen from the remarks of the Director of Education for the Transvaal: ⁴⁾ "The principals of schools from which children had been sent for treatment for bilharzia were requested to report on the physical and mental improvement of these cases after cure and the replies received show that approximately 75% of the cured show marked improvement mentally and in physique, this improvement being permanent. Some principals were so struck by the improvement in the pupils that had been cured

that they advocated examination for bilharziasis in all retarded pupils before anything else was done."

At Basrah, Hall ¹²⁹⁾ reported that the Schoolmasters there could not get "full value" out of the boys infected. In South Africa, with its quota of "poor whites", many of whom are definitely below the average "white" standard, both intellectually and in physique, the seriousness of this problem assumes alarming proportions. Comforting, perhaps, is the thought that for bilharzia at present there is a definite cure available.

In one case (J.L.) the boy was brought for examination on account of "not getting on well at school." As he was suffering from enlarged tonsils and adenoids, to this was attributed his difficulty at school. Though in the cases investigated a definite degree of mental retardation was only obvious in two of the boys, the impression, that it was not altogether absent in some of the others, was at times obtained. The boys whose cases are reviewed, as pointed out elsewhere, were of a better type of the community with regard to their general social standing, and this symptom and sign among them was not common; but among the lowest strata of the white races breeding in ever increasing numbers, restrained only by crude biological laws - high infant mortality, prematurity, idiocy, leading to an early demise - the "poor whites", it presents a most impor-

tant problem. In the treatment camps, most of the children were recruited from such sources and to them particularly does the Education Department report refer.

Anaemia.

The case of Mr. P.O., age 34, presents some interesting features for consideration. When first seen she had been practically bedridden for two months on account of extreme weakness. She further complained of shortness of breath on exertion, slight puffiness of the ankles, and occasional attacks of diarrhoea. In appearance she was very pale with a biscuit coloured tint to her complexion, and the diagnosis of Pernicious Anaemia was provisionally made. To confirm this the blood was examined but the picture presented a typical one of secondary anaemia, with an eosinophilia of 12%. The report read:

Red Cells.

Red blood corpuscles	2,800,000
Haemoglobin	30%
Colour Index54
Leucocytes	9,400

Numerous small corpuscles of various sizes and shapes.

No nucleated red cells or megaloblasts were seen.

White cells.

Polymorphs	57%
Eosinophils	12%
Lymphocytes	30%
Other cells	1%

As the patient had been resident in an area endemic for bilharzia, and as several cases with this infection were being treated at the time, the diagnosis of that condition was highly suggestive, and with it in view the urine was examined for ova. None were, however, found, and the next step was the examination of the faeces for other helminthic ova. To the great astonishment of the observer, eggs of bilharzia haematobia were abundantly present. No evidence of any other parasite infection was found at any time. That recovery was dramatic, after a course of intravenous sodium antimony tartrate injections, served to confirm the diagnosis. A rectal examination revealed nothing abnormal. A sigmoidoscopic examination was not attempted.

The outstanding features in her case, therefore, were

- (a) the marked anaemia, clinically simulating the Addisonian type,
- (b) the eosinophilia, which suggested the presence of a parasitic invasion,
- (c) the presence of ova of bilharzia haematobia in the faeces and
- (d) the remarkable recovery on treatment.

A few of the other cases appeared a little pale and sallow, but not much significance was attached to this, in young boys exposed to the tanning effect of the semi-tropical sun.

Girges ¹²³⁾ classifies the causes of anaemia as

- (i) toxaemia
- (ii) haemorrhage
- (iii) sepsis.

In the case of Mrs. P.O. there was no history of haemorrhage from the bowel or any other place, no obvious sepsis was discoverable, and it must be presumed that toxaemia resulting from the invasion of the worm was the cause. This opinion is further strengthened by recalling her predominant symptom - extreme weakness.

"Eosinophilia" according to Day, quoted by Byam and Archibald, "is present from the commencement of infestations", and Sharp ²²⁸⁾ writes that "undoubtedly a high eosinophilia and a positive complement fixation test are the two most frequent signs of the disease." Both these, however, particularly the latter, fall to the province of the laboratory worker rather than to the clinical undertakings of a general practitioner. Blood counts and complement fixation tests were not necessary to verify the diagnosis in the cases recounted, as the urine examination made it obvious in all except Mrs. P.O.; though no doubt, as probably occurs with most practitioners in South Africa, the diagnosis of many cases was missed.

Appendicitis.

Appendicitis as a lesion or event in bilharzia infected cases in South Africa is too common an occurrence ¹³⁾ to be merely incidental, and is therefore included here under the group of Symptoms. Two of

the cases under review were first diagnosed on the operating table from the appearance of the appendix. J. Harvey Pirie in ²⁰⁸⁾ five years found 20 appendices which on examination proved more or less heavily infected with *Schistosoma haematobia*. "The white nodules beneath the serous surface are," he points out, "commonly mistaken for tubercles, though the latter are less hard, glistening and porcelain like than schistosoma "tubercles". It is, personally, a known fact, that many surgeons in endemic areas in South Africa recognise the appearance at operation, just as readily as they do in the case of a malignant tumour of the bowels with metastases in the liver. The lesion is not of the hypertrophic type, as seen in tuberculosis with peritoneal proliferation, thus minimising the liability of perforation. Temple Mursell of the Johannesburg Hospital in 1912 recorded a case of such a happening. ¹⁹⁵⁾ The specimen is at present in the Hunterian Museum, London. ⁶⁶⁾ Cawston's reminder that in an endemic region the surgeon should always suspect schistosoma infection where in males or females there are ill-defined pains in the lower part of the abdomen, well merits attention.

Signs and symptoms of Advanced Disease.

These are rare in South Africa, the condition being of a milder nature than the type present in Egypt.

Chronic Cystitis with sepsis supervening is

rarely seen. When it does occur, great pain may be caused by the passage of clots of blood or plugs of coagulated pus.

Hydronephrosis from obstruction of the ureters by bilharzial lesions, though comparatively common in Egypt ¹⁴¹⁾ is not so in South Africa. Cases, however, have been recorded, among the post mortems performed by the staff of the South Africa Medical Research Institute. ¹³⁾

Cachexia. Though this is common in the late stages its occurrence in the early periods is often seen. In the camps at Zeerust and Rustenburg ⁸⁾ it was present as a symptom, without, unfortunately, evoking any comment or call for diminution in the initial doses of the drug given. Sharp, ²²⁸⁾ however, considers it a rare symptom in Natal.

Fistulae and malignant disease of the bladder are rarely seen in South Africa. So also are papillomata and the other late results that are so common in Egypt.

Special Symptoms and Signs.

Affection of the Female Genital Organs.

The only female case in the series analysed showed no signs of the infection referable to the genital organs, though such a site for the locality of lesions is not infrequent in South Africa. It may attack the vulva, forming warty or polypoid growths resembling venereal warts. The hymen and clitoris

may be destroyed by ulcers, which may simulate carcinoma. So also, is this the case, when the cervix is involved. In the vagina the common lesion is a sclerosis of the vaginal mucosa. The late Dr. R. Gibson, Gynaecologist at the Johannesburg Hospital, has never come across a case of Bilharzia infection of the uterus. ¹²²⁾ He also has recorded a case ¹²¹⁾ where the Fallopian tube and its mesosalpinx were infiltrated with ova of Schistosoma haematobia. Des Ligneris ¹⁰²⁾ in South Africa has recounted a case of bilharzia infection in the genital tract resulting in dysmenorrhoea, oligomenorrhoea, comparative sterility, and tubal pregnancy.

Calculi.

Small hard uric acid or oxalate stones are said to be common in Egypt. In South Africa it is by no means so. Mr. Beyers, ²⁰⁾ surgeon to the Johannesburg Hospital comments on the fact, that, whereas schistosomiasis is common among the Bantu tribes, calculi are rare. Cawston ⁵⁸⁾ however, says: "Careful examination of the urine of patients complaining of gravel often reveals the presence of ova, though the patient himself has seen no evidence of bilharzia for many years." This certainly was the experience of Harley when he examined the sons of Mr. Dunsterville of Port Elizabeth. ¹³²⁾ It must also be pointed out that while Mr. Beyer's statement

refers to the natives, Dr. Cawston's concerns the Europeans. In Sharp's opinion vesical calculi are not uncommon in South Africa. ²²⁸⁾ No cases of calculi were personally observed.

Nervous symptoms.

Apart from the slight mental retardation present in some of the cases, no other signs or symptoms referable to the nervous system were encountered. Epileptiform fits in bilharzia patients have been seen to cease after treatment with antimony tartrate. ²²⁸⁾

Ferguson pointed out that the ova may exist in many of the tissues or organs of the body, and due to their presence or to the resultant thickening of the membranes around the spinal cord may give rise to symptoms resembling tabes or disseminated sclerosis. ^{111, 112)}

Rectal symptoms.

Byam and Archibald quote Fairly as stating that [^]rectal symptoms are more common with Schistosoma haematobia than is generally supposed, and that although the faeces in these cases often is bloody, in many there are no signs whatever. Mrs. P.O. is a case illustrative of this. No special symptoms of any kind were complained of, to direct attention to such a possibility, indeed, apart from the presence of the ova in the faeces the diagnosis would have remained undetected. It might have been expected

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that the responsible helminth was the *Schistosoma mensoni*, but that was not the case. In this connection it is of interest to note the frequent presence of *S. haematobia* in the appendix in South Africa, ²⁰⁸⁾ and also that in Gambon, Nessmann and Tenzs; ¹⁹⁷⁾ Sinderson and Mills ²³⁰⁾ in Mesopotamia; and Leger ¹⁶²⁾ from the French Congo, report the prevalence of intestinal and rectal symptoms with *B. haematobia* infection, whereas vesical symptoms are rare.

Sharp ²²⁸⁾ believes the condition rare in S. Africa. Several cases that he has observed have given a history of dysentery since infection with bilharzia, but he has failed to find ova in the faeces of these cases.

Pulmonary symptoms.

Cawston ⁴⁹⁾ remarks that bronchitis may be one of the early symptoms of infection. That, the ova may be present in the lungs has long been known; ¹³⁾ Turner, ²⁵¹⁾ in 1910, found among the natives of the Rand gold mines that 64% of 28 cases dying of pulmonary complaints showed in their lungs ova of *S. haematobia*. Le Roux ¹⁶⁶⁾ found the adult worms in the pulmonary vessels of a sheep.

The case of "Piet" recorded was of interest. Piet, for two years before his condition was diagnosed and treated as a case of bilharzia, was subject to fairly frequent typical attacks of bronchial asthma.

On numerous occasions after the diagnosis of bilharzia was made the sputum, which was never blood-stained, was examined for ova, but none were found. Soon after treatment was commenced the attacks ceased and have not recurred since (as far as one is aware). A few peculiarities of his case merit attention. The attacks were usually worse when the haematuria was more severe. After each injection he had violent fits of coughing, terminating in, and relieved by vomiting. This latter symptom no doubt was reflexly produced by the straining, but whether the attack of coughing was, so to speak, a perverted attack of asthma, an idiosyncrasy to the drug, or merely even of psychical origin, was difficult to determine. Another perplexing symptom presented itself, further, to obscure the issue. Immediately after each injection he complained of a tingling sensation, up his arms and down to his toes. No dermatographia suggesting an urticarial type of lesion was ever found. Whether this last symptom mentioned can be taken to support the view that the coughing was an attack of asthma or whether the sign itself was of psychic origin was never satisfactorily determined.

Pigmentation.

In 1930, Sinderson ²³³⁾ described a peculiar butterfly shaped area of pigmentation on the face, in 20% of the cases admitted to the Royal Hospital, Bagdad, suffering from S. haematobia infection. The

pigmented area was dark brown in colour, on both cheeks and along the bridge and lateral aspect of the nose. As a result of this observation, the urines of cases demonstrating this sign were examined for bilharzia, and often with success. In South Africa no one has as yet recorded the presence of such a valuable sign.

DIAGNOSIS

The numerous cases in the literature where bilharziasis has been mistaken for some other condition serves to illustrate how difficult is the diagnosis when not suspected. Fabre ¹⁰⁶⁾ quotes cases where it was mistaken for abdominal tuberculosis; Pfister ¹⁰⁷⁾ where it was taken to be tubercular orchitis; the presence of renal calculus has often been suspected; ¹⁴¹⁾ so also, amoebic dysentery in Nigeria ²²⁹⁾ and Porto Rico; ⁷⁵⁾ and gonorrhoea no end of times. ¹³¹⁾

In endemic areas the presence of haematuria should always be an indication for microscopical examination of the urine. It is a curious psychological fact that an undergraduate when asked to enumerate the common causes of haematuria, will very often commence with "Bilharzia", whereas in point of fact, in actual practice, and where this would be most justifiable "Bilharzia" is the last diagnosis considered - even if thought of. In these areas any peculiar symptoms not otherwise explainable,

should prompt a search for ova. In the group of cases reviewed, ova were found in the urine of all, with the exception of Mrs. P.O.

The presence of an eosinophilia if discovered should also suggest a search. In tropical and semi-tropical countries, however, it is not at all uncommon to find many of the population infected with other helminthic parasites, thus making the presence of eosinophilia an indication, not a proof, of diagnosis of bilharzia. In the Transvaal, Watkins-Pitchford states, 10-19% of the individuals are subject to tape worm infestation with resultant eosinophilia. ²⁵²⁾

The presence of eosinophilia will usually only be revealed as a result of a routine blood examination. When present, and when there are no ova to be found in the urine, the faeces must be examined. The case of Mrs. P.O. serves to recommend this course.

Khalil and Salah El Din ¹⁵⁴⁾ advise for microscopical examination of the faeces three methods of obtaining the ova:

- (a) The selected smear of the faeces made on a glass slide.
- (b) From the precipitate in an Erlenmeyer flask, after concentrated salt solution has been added to the faeces, making the eggs sink to the bottom.
- (c) From the mucus adhering to the unvaselined rubber fingerstall, after a manual rectal examination.

In South Africa, however, infection with *Schistosoma mansoni* causing rectal symptoms is rare

and also those as a result of *Schistosoma haematobia* too, are not common.

The complement fixation test, ¹⁰⁸⁾ the intradermal test, ¹⁰⁹⁾ and the test of Tsykalis and Riegl ²⁵⁰⁾ of injecting $\frac{3}{4}$ - $1\frac{1}{2}$ grains of emetine as a provocative, dose to precipitate the discharge of ova, will be mentioned in the chapter dealing with treatment. Suffice it to say that the one sure, definite and positive proof of infection is the presence of the ova.

Lotzy ¹⁷⁴⁾ described a series of changes noticed on radiological examination of the vesical area and due to the presence of calcified ova - but he concludes that the appearances by themselves are not diagnostic, and must be confirmed with other observation.

Cystoscopic appearances are fairly constant and afford, to the experienced operator, a good indication as to the diagnosis. Minet ¹⁹³⁾ in his description of a series of cases, describes three stages.

- (a) Small yellow granulations, to be differentiated from tubercular nodules by their prominence. This appearance he considers as absolutely characteristic.
- (b) Infiltrated swellings of the mucosa, studded with yellowish granulations.
- (c) Fungating vegetations of the mucosa forming sessile tumours. It is possible by following a fold along its course in some instances to observe the gradual transition from infiltrated to congested mucosa to the fungating stage.

In areas where the condition is not endemic,

when confronted with a case of haematuria, all the causes of that symptom must be systematically reviewed. A blood examination in an obscure case of haemorrhage will doubtless be done as a routine and the presence of eosinophilia will further serve to direct attention to the search for ova.

CHAPTER IV.

THE TREATMENT OF SCHISTOSOMIASIS.

It seems surprising that, though the discovery of the existence of the parasite was made in 1851, it was not till 1881 that the first attempt was made to treat the disease. This was done by Probst, who used the liquid extract of the fern, *Fraxinus*. In this, the only method of treatment had been surgical - the removal of the worms in situ. In 1881, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern.

CHAPTER V.

TREATMENT OF SCHISTOSOMIASIS.

Probst's method was reported in 1881, and in 1882, a paper by Probst and Probst, in which they described the liquid extract of the fern, and its use in the treatment of the disease. In 1883, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern. In 1884, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern. In 1885, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern. In 1886, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern. In 1887, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern. In 1888, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern. In 1889, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern. In 1890, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern. In 1891, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern. In 1892, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern. In 1893, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern. In 1894, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern. In 1895, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern. In 1896, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern. In 1897, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern. In 1898, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern. In 1899, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern. In 1900, Probst, in his paper, "Ueber die Schistosomiasis," described his method of treatment with the liquid extract of the fern.

CHAPTER V.THE TREATMENT OF SCHISTOSOMIASIS.

It seems surprising that, though the discovery of the aetiology of Endemic Haematuria ^{23, 24, 25)} took place in 1851, it was not till 1885 that the first attempt was made to kill the worm. This was tried by Fouquet ¹¹⁵⁾ using the liquid extract of Male Fern. Previous to this, the most successful treatment had been surgical - when complications, such as stones, urinary fistulae, papillomata, tumours and kidney complications, such as hydro-nephrosis, pyelitis or pyelonephritis, were present.

Fouquet ¹¹⁵⁾ reported in 1888 that he had cured 48 cases; his treatment consisted of fifteen minims of the liquid extract of Male Fern administered three times a day one hour before meals; the treatment was continued for a maximum of fifteen days, and if after an interval symptoms still persisted, the treatment was resumed. This routine was continued for a maximum of three months.

For nearly thirty years this was the method of treatment with slight modification. As late as 1917 Zaiful advocated it, with the addition of buchu, sodium benzoate, urotropine and other urinary anti-septics, in spite of the fact that Briscoll ²⁹⁾ in January 1916 had reported that Male Fern did not cure

the disease.

In the meantime other methods were being tried thus Sonsino ²³⁵⁾ in 1885 reported that perchloride of mercury was being used in Egypt; Allen ²⁾ in Natal in 1888 advised the use of intravenous injections of alcoholic solutions of santonin; Sandwith ²²⁵⁾ in 1904 gave santonin alone or mixed with iodoform; he also quotes Dights as suggesting the injection of Hydrogen Bisulphide gas and carbon dioxide gas into the rectum or bladder to kill the schistosoma. Garcia Puellos ¹²⁰⁾ in 1911 cured a case of Bilharzia by electrargol; Conor ⁹⁶⁾ in 1911 recommended salvarsan injections, but Day and Richards ¹⁰¹⁾ the following year reported that it had no effect; quinine hydrochloride was advocated in 1911 by Tsuchiya ²⁴⁸⁾ for killing the adult Schistosoma japonica; Robertson ²¹⁹⁾ of South Africa in 1914 reported that thymobenzol cures Schistosomiasis; South African opinion was further represented by Cawston ³⁴⁾ in 1916 who recommended the use of hexamine and buchu; methylene blue and lavage with quinine were used by Briscole ²⁹⁾ in 1916 whilst in the same year Tootell ²⁴³⁾ reported good results from the administration of mercurochrome in Schistosomum japonica infection, but later recorded severe reactions from its use. ²⁴⁴⁾ During all this period, a mixture of buchu and hyoscyamus was given to all cases at the Qasr-el-Aini Hospital in Egypt.

Besides experimenting with the whole gamut of drugs and measures which might disinfect the urine or kill the worm within the human body, other forms of treatment were given a trial. Thomson of Hankow, quoted by Lambert (1910) ^{157, 158)} investigated the effect of Calcium Salts, and Hooton ¹⁴⁰⁾ in 1914 found that the exhibition of calcium chloride resulted in a cessation of the haematuria. The use of ionisation for the bladder lesions was advocated by Thompson ^{240, 241)} in 1914.

The effects of X-rays were tested by Kawamara, Kasama and Tanaka ¹⁴⁸⁾ in 1914, who found that the adult schistosoma were not influenced in any way.

Carbon Tetrachloride is another substance which had been put to the test in Bilharzia. Cawston ^{67, 68)} in 1928 suggested that one or more massive doses of Carbon Tetrachloride given at intervals sufficiently large to enable the system to recover completely, may be effective in producing a cure in certain cases.

No recent list of attempts made to combat any disease would be complete without the record of some one or other having employed diathermy. Bernard ¹⁸⁾ in 1928 supplemented antimony tartrate intravenously with diathermic coagulation of vesical lesions. He reports that this combination gave exceptionally rapid cures.

Of all these methods the drug emetine has been the most favourably accepted. The honour for the

priority of its introduction is a matter of dispute. Both Taamis ²⁴⁷⁾ and Tsykalas ²⁴⁹⁾ claim to have employed it in 1913. It was Diamantis ¹⁰⁴⁾ in 1916, however, who brought it to the notice of the medical world. Since then many have employed it with varying results.

In South Africa, Sharp ²²⁷⁾ in 1924 wrote:

"I have examined the urines of a large number of children in the schools of Natal who have undergone a course of emetine treatment and I have found that many of these cases pass viable ova in the urine although all the symptoms of bilharzia disease so far as the patient can observe have been absent since the cessation of treatment."

The conclusions derived from various reports may be summarised as follows:

1. It is preferably injected intravenously. No complications result from this method of administration should any of it escape into the surrounding tissues.
2. When injected more than once at the same site intramuscularly or subcutaneously, "intense irritation or slight inflammation may ensue." ¹⁵⁵⁾
3. Its toxicity in some cases is very marked, especially as large doses are required. ⁸⁶⁾ Amongst the minor symptoms resulting are tachycardia (Cawston ⁶⁰⁾ considers that

this makes it risky), hypotension, anorexia, diminished reflexes, vomiting, arrhythmia and dyspnoea. Those necessitating immediate cessation of its use are diminution of the urine, the appearance of albumin and casts, neuritis (which is most distressing to the patient), local muscular paralysis especially of the neck muscles, jaundice and coma. Sudden death may also occur. It is therefore not free from danger.

4. Its use in the Anthelmintic Hospitals 155)
 in Egypt has been limited "to children and 'fat females' where the veins are small and deeply seated and do not allow safe intravenous Tartar Emetic injections; when intestinal bilharziasis is complicated by amoebic dysentery; where there is intolerance to Tartar Emetic or other antimony preparations,"

As is the case, throughout medicine, where no specific treatment is available, the number of reported cures soon mounts up. Furthermore, in the case of Schistosomiasis it must be remembered that even without treatment the ova at times disappear temporarily or even permanently, as does also the most noticeable symptom, the haematuria. In addition when it is borne in mind that most of the reports of successes were on individual cases only, with no

sustained and prolonged attempts to examine microscopically for ova, the value of any one of these cures becomes apparent. Further to appreciate the value of any of these lines of attack on the schistosoma one need but realise that these methods (with the exception of emetine) have all been dispensed with.

THE ANTIMONY TREATMENT.

The use of Tartar Emetic intravenously was first attempted by Broden and Rodhain ³¹⁾ in 1908 for Trypanosomiasis, and to them the honour thus belongs of conferring an untold boon on humanity. In 1912 McDonagh ¹⁸⁷⁾ of London used intravenous antimony in bilharziosis, but owing to the fact that he recorded this in his book entitled The Biology and Treatment of Venereal Disease, publishes in 1915, it escaped the notice of those medical men to whom it might have been of interest. When in 1918 ^{79,80)} Christopherson from Khartoum recorded his success with Tartar Emetic and aroused widespread interest with his results, McDonagh wrote to the Lancet ¹⁸⁶⁾ verifying its efficacy: "I only used it empirically in view of the good results obtained in other diseases caused by animal parasites," he states. Later, in 1923, McDonagh ¹⁸⁸⁾ claimed priority, but it is obvious by the attempts to broadcast the information gained

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from the cases treated at Khartoum and it was Christopherson who first realised the significance of the Tartar Emetic treatment. Christopherson⁸¹⁾ in 1919 said: "It is stated by the highest authority (referring to Manson's Textbook on Tropical Diseases, 6th Edition, 1918) that no direct or other means is known by which the Schistosomum can be destroyed. In other words, there is no known cure for Bilharziasis. This was true, excepting the fact that most cases of Bilziазiasis are cured by time. Let that pass. Now we think there is a cure and apparently a sure cure - antimony tartrate."

From that time onwards antimony tartrate has been the standard treatment for Bilharziasis. Christopherson in 1923, after having been able to watch its universal adoption for some years, was able to pronounce:⁸⁴⁾ "There appears to be no drug in the British Pharmacopoea more specific than, and so reliable in its action as antimony tartrate."

Potassium Antimony Tartrate and Sodium Antimony Tartrate.

Christopherson^{79,80)} in 1918 advised the use of potassium antimony tartrate. In 1920 Diaie¹⁰³⁾ suggested substitution of sodium antimony tartrate, owing to the fact that this was less toxic. In the same year Harkness,¹³⁰⁾ a medical practitioner in London, who had undergone a course of injections of

sodium antimony tartrate, wrote in a letter to the British Medical Journal: "Personally I experienced no inconvenience during the course of treatment, but in point of fact owing to the exigencies of my profession, I carried on with my work as usual." The efficacy and preferability of the sodium salt were further reported on by Nishi in 1923¹⁹⁸⁾ and Meleny in 1924.¹⁹⁰⁾

In South Africa Cawston in 1924⁵⁶⁾ recommended the potassium salt, stating that it is less toxic and that a small total amount is required. In 1930 he adds:⁷⁴⁾ "... and it is further great encouragement to me to know that veterinary surgeons continue to employ the potassium salt in spite of all that is claimed by leading physicians and others that the sodium salt is to be preferred."

In Egypt sodium antimony tartrate was employed on a large scale in 1923¹⁵⁵⁾ but its use was discontinued. "Unfortunately the sodium salt is not manufactured in sufficiently big amounts and so it is difficult to secure and is more expensive. In addition it is apparently less stable than tartar emetic." (Khalil)¹⁵⁵⁾

The Public Health Department of the Union of South Africa in 1929²³⁷⁾ advised sodium antimony tartrate in the form of Burroughs Wellcome & Company's "Soloid" Antimonii Tartratis Comp. No. 1 or No.2, the former for mass and the latter for individual treatment.

Apart from the few instances which will be quoted below, it is impossible to estimate the relative frequency of employment of the two salts in South Africa. Judging by the fact that the circular on standard treatment issued by the South African Public Health Department was "drawn up by experts consulted by the Department," ²³⁷⁾ the sodium compound is the evidently more favoured one. No description resulting from its use can, however, be traced in the literature.

An attempt is herewith made to supply a resume of thirty-four cases treated by sodium antimonium tartrate. Uniformly good results were obtained in this series. This is attributed to certain factors which will now be described in detail.

Choice of Preparation.

The preparation used in all the cases treated was Burroughs, Wellcome & Company's Soloid No. 2.

Its composition being:

R.
 Antimonii et Sodii Tartratis gr. i
 Sodii chloridi gr. 11/20

It was realised that owing to supplies of fresh drugs not being always obtainable in S. Africa - the "stock-in-hand" at all chemist shops included a great number of preparations which had been influenced by age and by the hot climate - it was essential to use care and judgment in prescribing. This cautious outlook should be a matter of concern to all

practitioners, but particularly so to South African medical men. The practitioner who is keen on discovering the exact value of a line of treatment should assure himself, as far as possible, that his prescription will be dispensed from preparations made by a reliable firm, that it should be properly standardised and proved, and of recent manufacture.

That this in South Africa is a very important matter may be judged by the fact that Le Roux, as recently as 1929, ¹⁶⁶⁾ working at the Onderstepoort Laboratory, Pretoria, used a preparation of Antimony which had been in stock for two years, and which had changed to an insoluble mixture producing a reddish deposit when dissolved. One has on many occasions been supplied with tablets which needed forcible beating with a hammer to break them! It is obvious that any drug prescribed may easily, if in liquid form, have lost its potency, or altered in toxicity, and tablets have been noticed to pass intact through the alimentary canal. Is it to be wondered at that in many cases results are anticipated and predicted, and nothing happens?

The Soloid No. 2. was chosen with these facts in mind. As at no time were any marked toxic symptoms noticed from the preparation, its administration was persisted in. This evidently, as has already been remarked, has been the experience of the "experts consulted by the Department (of Public Health of the Union of South Africa) as a guide to the standard

treatment of Bilharzia." 237)

Preparation of Solution for injection.

There is hardly any scope in the type of practice under review to test for the presence of impurities such as lead, arsenic, copper, iron, chlorides or sulphates. Khalil ¹⁵⁵⁾ states "It was noted in Egypt that different consignments of Tartar Emetic which comply with the British Pharmacopoea specifications produce varying symptoms on the patients when injected. This is quite apparent when a large number of individuals, i.e. 200 or more are injected, as is commonly the case in the Anthelmintic Hospitals in Egypt. An increase in the incidence of cough and its severity as well as a rise in temperature, and later the appearance of herpes round the mouth, sometimes attract the attention when a new consignment is used.

"Investigations led to finding in the offending samples traces of lead and arsenic in amounts varying from 5 to 40 parts per million. These impurities by themselves do not explain the bad effects produced, but their presence may be taken as indication of other unknown impurities which increase the toxicity of the drug. Such impurities do not matter when the drug is administered by mouth..... For intravenous administration a more rigorous degree of purity is demanded. In Egypt it has been found advisable to control the purity of all the Tartar Emetic

imported into the country. No consignment is admitted unless it complies with the following specifications." He then details the tests employed for the impurities already mentioned.

It is obvious that without the necessary facilities at one's disposal, one must be on the careful look-out for any departure from normal in the appearance of the solution, if harmful effects and complications are to be avoided.

The Soloid No. 2. as a rule made up into a colourless and perfectly clear solution. If at any time there was any alteration in the colour - a faintly yellowish tint was observed on quite a few occasions - or if small particles were seen floating about in the solution, as was the case on many occasions, it was at once discarded.

Much importance must be attached to this precaution, though Khalil is the only one who remarks on it. Turbidity he says, may be caused by disintegration of the salt into an oxide of antimony which is very toxic if injected intravenously, and the sterilised solution if not clear and free from particles must not be used. Even in the circular already referred to, issued by the Public Health Department in 1929 ²³⁷⁾ on the standard treatment of bilharzia, there is no mention of this small but very important detail.

In discussing the relative merits of the Potassium and Sodium Salts, Khalil ¹⁵⁵⁾ states:

"It (the sodium salt) is not as stable as potassium salt. It more frequently decomposes on boiling, producing a white precipitate of Antimony Oxide. If this occurs a severe reaction follows its injection into the body, manifested by paroxysms of coughing, a sharp rise of temperature, and the appearance of herpes around the mouth. One particular consignment had a slightly yellowish colour, but conformed to the chemical specification. The drug ought to be perfectly white." This yellowish colour of the drug itself was not noticed - as already stated - a faintly yellowish tint was the reason for discarding the solution on quite a few occasions.

The Soloid No. 2. has to be dissolved in 4 c.c. of water, giving a concentration of $\frac{1}{4}$ grain of sodium antimony tartrate to 1 c.c. It was found that when boiling this solution in a small dish there was a tendency for spluttering to occur, with a resultant precipitation of some of the salt on the sides of the receptacle, thus altering the concentration. To obviate this, ampoules containing 5 c.c. of distilled water were used. After filing through the neck of the ampoule, one c.c. of the water was drawn off in a sterilised syringe, a slight scratch was made at the top level of the remaining fluid and the 'soloid' was dropped into the ampoule. This was then placed upright in the water of the sterilizer, with improvised weights to keep

it from being toppled over by the force of the water boiling. When sterilised, the quantity of water evaporated was made up from the 1 c.c. originally drawn off, the scratch acting as an indicator.

Khalil ¹⁵⁵⁾ agrees with the importance of this precaution, remarking, "It is advisable to mark the top (level) of the fluid and to add sterile water after sterilization to bring it back to its original volume." The wisdom of this procedure was appreciated on reading of a case of sudden death reported by Khalil, to which reference is later made.

Freshness of the Solution.

The preparation and sterilization of the solution was commenced about half an hour before the patient was expected. By this method it was assured that a fresh solution was used for each injection; if for any reason the injection was not given - as for example, if the patient did not present himself on the day appointed, the ampoule was discarded. The principle of discarding solutions of doubtful purity involved a negligible expenditure. 25 Soloids cost two shillings - roughly one penny each, and the ampoule about five pence.

The Union of South Africa Health Department in 1929 ²³⁷⁾ lays stress that "on no account should the solution be used after it is twelve hours old."

Khalil ¹⁵⁵⁾ agrees with the preferability of injecting the solution on the same day, but on the other hand states that the potassium salt may be kept for as

long as three days. "Old solutions (i.e. older than three days) may cause toxic symptoms. The explanation is not definitely known. It has been suggested that isomeric compounds which are more toxic are slowly formed in the solution." Cawston,⁷⁰⁾ however, using potassium tartrate as well, emphasises the need for the preparation of the solution immediately prior to injection. For this reason too, "Ampoules" and other read-made solutions sold under various trade names are usually unreliable and should not be used.

Warmth of the Solution.

By adopting the procedure outlined it was possible to inject the solution at about body temperature. At the Anthelmintic Hospitals in Egypt also, attention is given to this point;¹⁵⁵⁾ collapse, it is stated, may follow the injection of a too warm solution.

Technique of Injection.

Christopherson⁸¹⁾ in 1919 in his second article on the use of antimony tartrate in Bilharziasis says: "I will not discuss the local difficulties and the dangers of injections. It is sufficient to say that when accidents occur they are generally due to faulty technique."

The technique that was adopted in all the cases treated will now be described.

The Syringe and needles.

By now it is common knowledge that a glass-barrelled syringe should be used for all intravenous injections. Nevertheless, in 1928 the author was consulted by an adult male who had been undergoing a course of injections of Salvarsan. A metal syringe had been employed. On complaining of severe pain and swelling after each injection he was informed that "this was a sure sign that it was taking effect." The result was that the veins at the bend of the elbows were entirely obliterated.

The ideal syringe was found to be one whose piston did not require too much force in pushing down - resulting in a jerky injection and displacement of the needle point from the vein - but yet on the other hand not so loose as to slip when unsupported.

The care that was given the syringe was proper sterilization before use and thorough cleansing after. Details of this nature are simple in a Hospital or Nursing Home, or when there is a trained nurse in attendance at the consulting rooms. In South Africa one has to rely in most cases on one's own initiative and adaptability. A small sterilizer heated by a methylated spirit lamp served well for sterilizing syringes, needles, etc. The washing of the syringe in cold water after use was found

to be essential - not in warmth sufficient to coagulate any serum if blood had been drawn into the syringe and so making it difficult to remove the piston. This applied more to the needle - drawing up cold water through it, blowing through it with a small hand bulb syringe, and dipping into absolute alcohol and drying over a spirit flame was the method adopted. In this way a favourite needle was made to last indefinitely. It is noticed that the Union Health Department in the 1929 circular advised the use of a Higgenson's Syringe to blow through the needle, ²³⁷⁾ but this would obviously be unwieldy.

It was soon realised that a sharp pointed needle made the difference between an easy, clean and quick injection and a belaboured, exasperating one. The confidence imparted to the patient by a quick and almost painless entry was found to be worth the extra trouble of honing the needle to a fine point with symmetric curves and examining it with a magnifying glass. Particularly does this apply in the case of children, where injections have to be repeated. The art of honing was learnt from an itinerant cutler who toured the South African towns and villages periodically to sharpen the knives, scissors, etc. of medical men and others requiring his services. The cost of tuition was the price of the stone, overpaid for but well worth the subsequent benefit and satisfaction derived therefrom. The length of the bevel

was carefully adjusted so that the liability of the point being partly in and partly out of the vein was avoided. This is an easy and serious mistake - blood is drawn up into the syringe and still some of the antimony is injected into the surrounding tissue, causing local abscess and perhaps necrosis. To avoid this a combination of the following factors was adopted: a short bevel, a short needle, of medium bore (such as a B.W. & Co. No. 71 or No. 23 hypodermic needle), the insertion of the needle in an upward direction, and piercing the vein alongside and above it more than directly into it, with the bevel upwards, i.e. towards the skin. It was not necessary to feel whether the point of the needle was inside the vein - the slightest movement, particularly in the small veins of a child, was sufficient to alter a correct insertion.

Position of the Patient.

It was insisted that the patient should lie down with the arm extended and supported by a chair. It was first the custom to sit down on the chair and allow the patient to rest the arm on the operator's knee, but this was found inconvenient if for any reason one had to move. The Union Health Department ²³⁷⁾ advise the lying down position, whereas Khalil states that this is not at all necessary; he, however, insists on his assistants standing up,

whilst giving the injection, with the patient sitting on a chair.

Tourniquet.

A rubber catheter served well as a tourniquet - the one end of the catheter was doubled and slipped under the other end, and this allowed of the least disturbance of the arm when pulling gently on the one end of the knot to loosen it. With slight practice the exact tightness with which to apply the catheter was soon discovered - if too tight there was a tendency for the arm not only to feel uncomfortable but also to become blue.

The injection.

The vein usually chosen for the injection was the medium basilic or median cephalic in the region of the cubital fossa and the skin in this region was sterilised by painting with tincture of iodine. Khalil ¹⁵⁵⁾ suggests penetrating a vein near its bifurcation or its junction with another vein, as it is more fixed there; this was realised, but on a few occasions greater resistance was encountered at these points, and the reason was thought to be the encountering of a valve, so that subsequent penetrations were not made too near these points of greater fixation. Whether this explanation is correct is not known; reference to this has not been discovered in the literature. The gentle

but firm pressure by the left thumb was found to be sufficient to keep the vein from moving about under the skin.

On piercing the vein as already described and getting a free flow of blood into the syringe either by its own pressure or an easy and gentle slight retraction on the "cap" of the piston, the catheter was gently loosened and the piston slowly pressed home.

No more solution was actually drawn into the syringe originally than was intended for injection as it was felt that, firstly, a smaller syringe was easier to manipulate, and secondly, there was the added security of not giving an overdose.

That this was a wise precaution is illustrated by a case of sudden death reported by Khalil: ¹⁵⁵⁾

"A boy of 12 years old was given 8 injections of Tartar Emetic for Schistosomiasis, when he suddenly died for no apparent cause. On investigation, it was observed that the treating medical officer gave the injections while he was sitting down with the patient standing in front of him. The result of this was that the blood flowing into the syringe when the needle entered the vein came to rest on the top of the piston, which was low. When the fluid was injected the medical officer, although intending to give a smaller dose than the 2 c.c. which was present in the syringe, pushed the piston home to the re-

quired mark, but the fluid remaining in the syringe was often nothing but blood, and thus the child had often received a full adult dose. If the medical man gave the injection while he was standing, as he ought to have done, the blood finding its way into the syringe would have been the first to go back into the vein when injecting."

From this occurrence certain conclusions can be drawn.

(1) That the obvious manner in which to prevent an occurrence of this description is not to fill the syringe with more of the solution than is intended for injection.

(2) The great toxicity of antimony in over-dosage.

(3) That it is essential to consider the smallest details in the intravenous administration of antimony.

In Egypt, owing to the fact that a great number of medical practitioners spend the major portion of the day giving injections the smallest detail has been investigated and recorded.

That the small details are worthy of publishing, particularly in South Africa, is a well known fact to the wirtter. Medical men have been encountered in the smaller villages who are chary of giving even a hypodermic injection, let alone an intravenous. Dr. Orenstein, ²⁰¹⁾ the President of the South African

Medical Association, in a paper read before the Plenary Meeting, Third Annual Scientific Meeting at Durban in July 1930, discussing the value of the "camps" for mass treatment, said: "It was also shown that medical men with little previous experience in intravenous injection of drugs easily learn the technique of administration and can be relied upon to do this work with perfect safety." From this can be seen that there are medical practitioners actually in endemic areas - the camps are held in the worst of the endemic areas - with "little previous experience in intravenous injections." That it is easy to learn the technique is admitted, but the operators should be aware of the minute details so that they can guard against the many pitfalls.

Correct Estimation of the Dosage.

In arriving at a correct estimation of dosage, certain factors had to be considered. These were:

- (A) 1. the initial dose.
2. The amounts of increase in individual doses.
3. The interval between injections.
4. The maximum single dose.
5. The total dosage.

As all these factors were judged by observations made before and during the treatment in each individual case and as consideration of each of these influencing observations would entail reiteration, it is

considered advisable to mention them as a group. Wherever applicable the following observations were noted:

- (B) 1. Age of patient.
2. Physical condition of patient - judged clinically, as to weight, debility, anaemia, stature, development.
3. Reactions to each individual or to successive injections:
- (a) with regard to toxic symptoms;
- (b) with regard to improvement of symptoms and signs.

Each item in Group (A) was influenced by some of the observations applicable to it in Group (B).

The following facts have been taken from various authors with regard to total dosage, etc. (A) and influencing facts (B):

1. Christopherson in 1918 ^{79,80)} advised grains 25-30 (potassium salt).
2. Christopherson in 1919 ⁸¹⁾ said "the total of grains 25-30 for a full course of injections which we have elsewhere laid down was suggested rather as a maximum dose available in one course."
3. Cawston ⁴⁶⁾ in 1920 April used $5\frac{3}{4}$ - $12\frac{3}{4}$ gr. (potassium salt) in cases reported.
4. Cawston ⁴⁸⁾ in 1920 August used $6\frac{5}{16}$ - 12 gr. in another series.
5. Lansbury and Coleman ¹⁶¹⁾ employed a total dosage of 20 grs., decreased in weak adult males and in women; for children the total amount was greatly reduced.
6. Cawston ⁵⁶⁾ in 1924 reports $12\frac{1}{6}$ - 14 gr. as total dosage.
7. Lampe ¹⁵⁹⁾ in 1926 found that the total amount of drug varies widely for different individuals. He doubts, therefore,

whether it is wise to inject all patients with a fixed amount.

- 70)
8. Cawston in 1930 prefers the dosage according to the age and the severity of infection to that corresponding to the patient's weight, experience teaching that those with a heavy infection tolerate unusually heavy doses.
- 201)
9. Orenstein in 1930 states that children of from 12 - 16 years of age can be started with $\frac{1}{2}$ grain to a maximum of between $1\frac{1}{2}$ grs. to $2\frac{1}{2}$ grs. per dose. The total amount to be administered is about 20 grs. to a child, and 25 - 30 grs. to an adult.
- 77)
10. Charlier in 1930 cured 36 out of 41 children with a total dosage of 0.5 grams.

155)

In Egypt, where potassium antimony tartrate is used, the dose is estimated according to body weight. 60 kilograms are taken as the standard body weight to receive the routine treatment. Patients of lesser weight are given a proportionately smaller dose. It is added that "since this routine was adopted in the Anthelmintic Hospitals, the number of accidents due to over-dose was appreciably reduced. The total dosage generally necessary to cure an adult is 1.5 grams to 2 grams (roughly $22\frac{1}{2}$ grains to 30 grains). The course consists of 12 injections given on alternate days. The first dose is $\frac{1}{2}$ grain, the next 1 grain, the next $1\frac{1}{2}$ grains, and then 9 injections of 2 grains. The full course of treatment lasts 4 weeks - three injections per week. The rules are qualified by the statement that "there are individual variations."

The dosage of sodium antimony tartrate, as

advised by the Union of South African Public Health Department ²³⁷⁾ in 1929, for use in camps for mass treatment, is calculated according to the patient's weight - 0.002 gram antimony tartrate per kilo body weight. As this is the only available complete record of dosage for treatment with the same compound as that used in the series of cases here reviewed, an abstract from records of the 34 cases treated is given below, and compared with "the standard treatment" advised. The figures represent amounts in grains; the amounts advised by the South African Health Department are given in red.

Age.	First Dose	In-creas-ed by	Maximum dose.	Total dose.
8-12	$\frac{1}{4}$ $\frac{1}{4}$	$\frac{1}{4}$ $\frac{1}{4}$	1- $1\frac{1}{4}$ 1- $1\frac{1}{4}$	12-18 18-20
12-16	$\frac{1}{4}$ $\frac{1}{4}$	$\frac{1}{4}$ $\frac{1}{4}$	$1\frac{1}{4}$ - $1\frac{1}{2}$ $1\frac{1}{2}$	15-18 18-20
16-20	$\frac{1}{2}$ $\frac{1}{2}$ - $\frac{3}{4}$	$\frac{1}{4}$ $\frac{1}{2}$	$1\frac{1}{2}$ $1\frac{1}{2}$ -2	15-20 20
20-25	$\frac{1}{2}$ $\frac{1}{2}$ -1	$\frac{1}{2}$ $\frac{1}{2}$	$1\frac{1}{2}$ -2 2- $2\frac{1}{2}$	18-20 20-30
Adults (Male)	$\frac{1}{2}$	$\frac{1}{2}$	2 2- $2\frac{1}{2}$	20-25 25-30
Female (1)	$\frac{1}{4}$	$\frac{1}{4}$	$1\frac{1}{2}$	19

In arriving at the dosage advised the Public Health Department considered the following factors:

1. In children of average age/weight relation the age may be followed for convenience; where the patient's weight is considerably below normal for age he is classed as in a lower age group.

2. The doses quoted (in red) are for "average healthy children" or "average healthy persons."

Summary of Treatment adopted.

1. For Adults: an initial dose of $\frac{1}{2}$ grain, increased by $\frac{1}{2}$ grain up to a maximum of 2 grains with a total of 20-25 grains.

In the one adult female case, the treatment was modified, as is recorded.

2. For Children: here the principle was, "the younger the child the smaller the amounts; the poorer-nourished the child, the smaller the amounts". Each case was judged on its merits.

It will be noticed from the original table that the dosage used in this series were smaller than those recommended by the Union Health Department, but that still smaller doses have been used with apparent success by other observers.

With the smaller doses given it was found possible in most cases to give the first three to four injections on consecutive days and then on alternate days.

Duration of Treatment.

This in Egypt ¹⁵⁵⁾ in four weeks; in the camps in South Africa evidently up to 6 weeks; Christopher in 1926 considered a full course of treatment to last 4-5 weeks. In the cases here reviewed the average duration of treatment was about 1 month, but in one case it was found advisable to extend this even to as long as 41 days and in another to 7 weeks.

Realisation of Significance of Contra-indications.

In the cases encountered in practice, and on which one's experience is based, none were found to be of such a nature as to warrant the opinion that "here is a case where the use of intravenous antimony is contra-indicated." Perhaps the number met with was too small, or perhaps the diagnosis of Bilharzia was overlooked in the concentration on the major condition for which the patient was receiving treatment. Be that as it may, the only semblance of a contra-indication - and this was formulated from the teaching one had received on the application of drugs to the feeble and the young, and after this from the experience that this method was crowned with success and with freedom from complications - was debility and youth. Such "semblance of a contra-indication" was countered not by refusing the patient antimony tartrate, but by reducing the initial doses, by the gradual careful increase in the individual dosage, and by the use of what was considered to be a minimal maximum total quantity.

With the adoption of this procedure it was found that in most cases where debility was present there was a marked improvement. To this further reference will be made later when describing the effects of treatment.

Heart disease - by which presumably is meant

heart failure - is stated by all writers, beginning with Christopherson,⁸⁴⁾ to be a contra-indication. No such case was encountered; none of the cases that had been treated subsequently developed heart failure with a relapse of the bilharzia infection, so that the occasion did not arise in which a decision would have been necessary as to what line of treatment to adopt.

Renal disease - is another condition stated to be a contra-indication.⁸⁴⁾ The diagnosis of this has obviously to be made from the presence of casts and from other tests of renal efficacy, as owing to the passage of blood the mere presence of albumin is of no significance. Davies of the Anglo-Egyptian Sudan, in the Transactions of the Royal Society of Tropical Medicine, 1927, goes as far as to say that only those urines showing albumin need examination for ova of schistosoma. Khalil¹⁵⁵⁾ says that serious affection of the kidney is an important contra-indication as the antimony is principally excreted through this organ.¹⁹⁹⁾ Nogue and Boulay however found that in 22 cases of "nephritis with bilharzia" treatment with tartar emetic cured the nephritis.

Khalil¹⁵⁵⁾ states that jaundice, fevers or a rise of temperature from any cause, contra-indicate the employment of tartar emetic. Pregnancy, he adds, is not a contra-indication, as many pregnant

women were successfully treated at Qasr-el-Aini Hospital, having been, however, under constant observation. No comments can be made on these conditions for the reasons already stated - that none of these were met with. In Egypt there are a sufficient number of cases, amongst which, some must be found to be in a class by themselves, but in spite of this Christopherson ⁸⁴⁾ states: "It is true that a few persons cannot take tartar emetic (idiosyncrasy) a few with collapsed or small veins cannot be given it, a few are too advanced in their illness and too weak to have it, a few have cardiac or renal disease and cannot with safety be given it, but the total of all such cases is small."

There is evidently one condition which is according to Khalil ¹⁵⁵⁾ an important contra-indication, namely, chronic schistosomiasis without living ova being discharged. One case was seen where a general debilitated condition necessitated a complete routine examination, including an examination of the stool, which was reported by the South African Institute for Medical Research as containing calcified ova of bilharzia. A course of tartar emetic injections had no effect on the condition.

As the propaganda campaign in South Africa is becoming more intensive and as the condition is becoming better known, both amongst the public and amongst the medical profession, and as no reference

to this can be found in any of the South African literature, it is perhaps as well to quote Khalil ¹⁵⁵⁾ in full: "Cases of chronic schistosomiasis not discharging living ova should not be treated. This rule is often neglected with serious consequences. Chronic schistosomiasis cases retain a large number of dead and calcified ova in the walls of the urinary and intestinal tract as the case may be. As a result of one course of treatment the worms may be killed and living ova cease to appear in the excreta. The symptoms of the patient may or may not be relieved as the treatment will exert very little influence on the pathological lesions beyond the cessation of more aggravating ova and toxins, forming thus favouring natural cure. These cases in Egypt, feeling unrelieved, seek other medical advice. The excreta are examined and often the presence of ova is reported. These are the dead calcified ova gradually ulcerating into the lumen of the affected organ. Without ascertaining the viability of the ova, the patient is submitted to another course of treatment. It is not infrequent to find these unfortunate people with a record of 80 to 100 injections of tartar emetic or more. The drug here serves no useful purpose. On the contrary, they begin to suffer from persistent asthenia and debility, due to a certain extent to chronic tartar emetic poisoning. They improve on the cessation

of the treatment. One cannot emphasise enough the dictum that specific anti-schistosomiasis treatment must not be given unless viable ova have been demonstrated, indicating the presence of active schistosomiasis due to living adult worms."

COMPLICATIONS OF TREATMENT.

Local Complication of Injection.

The toxicity of antimony has repeatedly been stressed by Christopherson and others. Throughout the whole series of injections there was only one instance of an abscess forming. This occurred in the patient, Mrs. P.O. in whose case, owing to the emaciated and debilitated condition it was exceedingly difficult to effect a satisfactory entry into a vein. During the second injection she complained of pain, and simultaneously, a filling up of the tissues around the vein was noticed. The needle was at once withdrawn and an attempt was made to "milk" out the small amount that had been injected around the vein. A small indurated mass formed at the site, but fortunately resolved, on the application of hot fomentations, without any further complication.

In about four cases, however, where the same vein had to be used for the injections, it was noticed that the site of entry became inflamed and

tender. This was explained as being due to the actual trauma. That it was not due to irritation of antimony is certain as the needle was washed with sterilised water after the air had been expelled from the syringe. It was not noticed when the right and left arm were used alternately. Innes¹⁴³⁾ describes the same effect after each injection, whether in the same arm or not. He explains it as an idiosyncrasy on the part of the patient to antimony.

Necrosis and sloughing were not encountered as the result of antimony tartrate, but a colleague practicing in the Pretoria District reported the case of a boy he had seen with necrosis of the head of the radius, as the result of a faulty injection.

Khalil¹⁵⁵⁾ estimates the incidence of faulty injections at the Anthelmintic Hospital of Egypt, resulting in inflammation of varying degrees of severity as 5%. He mentions a few cases in which necrosis and sloughing necessitated amputations to save the patient's life and two instances of traumatic aneurysm of the brachial artery.

General Toxic effects.

That toxic effects may result from each individual injection or from the total amount of antimony administered is a warning note that has been sounded time and again.

86)

Christopherson in 1924 points out that one of the contra indications to treatment is debility; the same authority in a letter to the South African Medical Record in 1919 states "The treatment requires care and judgment If anything goes amiss, the operator should ask himself whether there is anything wrong in his technique. If anything goes amiss, it is more likely to be the fault of the operator than the fault of the patient or the remedy." And in the Lancet ⁸¹⁾ in 1919, says "They (accidents) will not occur if the following elementary facts are realised.. that the drug is a powerful one, and must be used with caution."

Uniformly good results free from toxic effects have not been recorded by all who have used sodium antimony tartrate in South Africa. The most illustrative example is the experience at the camps for mass treatment in the Transvaal.

In the report on the first camp at Zeerust, in August - September and December 1926 - January 1927, where "mass treatment" of school children was carried out by the school medical officers of the Transvaal Education Department sponsored by the Union Health Department, it is stated that the urines of fifty-four out of seventy-one children, were found to be free of blood and ova "while the remainder either left before completion of the course, or still showed signs of the disease." The report goes on to say,

"Although the results were not as satisfactory as had been hoped for, valuable experience in technique and in organisation had been gained. In December 1927 - January 1928, a "camp" was organised on better lines at Rustenburg, where sixty-six school children were treated. Practically all were found to be markedly ill-nourished and cachectic, and many had malaria as well From various causes fifteen of those who began treatment left before the course was completed (eight left of themselves, in six others treatment was stopped owing to unfavourable symptoms: one died Ages varied from eight to twenty years, and the "course" extended over thirty-three days. The initial dose for all was 1 grain of sodium antimony tartrate (Burroughs Wellcome & Company's Soloids), being increased in those between eight and thirteen years by $\frac{1}{4}$ grain daily to a maximum dose of $2\frac{1}{4}$ grains. In those aged from fourteen to twenty years the daily dose was increased by $\frac{1}{2}$ grain to a maximum of $2\frac{1}{2}$ grains. A total of twenty-five to thirty grains of the drug was given to each of fifty-one children who completed the course, and at the end it was found that forty-six (i.e. roughly 92%) showed neither blood nor ova in the urine, but five still showed living ova; in these five subsequent treatment was successful."

"Toxic symptoms (e.g. coughing, vomiting, abdominal pain, evanescent rash, toothache and

gingivitis) were noticed in the majority of the patients, especially towards the end of the period of treatment, due to the cumulative action of the drug. The malnutrition and cachexia from which so many of the children suffered were considered to account for the relative severity of these symptoms."

Before remarking on this very serious and significant report, it is as well to note the instructions given both in Burroughs Wellcome & Company's Medical Diary, and in the pamphlet packed around each bottle of "Soloids": "Sodium Antimony Tartrate. Used by intravenous injection against leishmaniasis (Kala Azar) and bilharziasis. Injected intravenously in doses of gr. $\frac{1}{2}$, gradually increased to gr. $2\frac{1}{2}$ daily for the first five days, and the remaining injections on alternate days, or all the injections may be given on alternate days. In cases of bilharziasis, a total of 25 gr. to 30 gr. and in Kala Azar a total of 50 gr. or more is required. Gr. $2\frac{1}{2}$ is considered the full dose of an adult; some patients cannot take this amount. Smaller doses should be used for children."

In spite of these instructions it is noticed that in the second "CAMP" at Rustenburg, after having gained "valuable experience in technique," the initial dose of all was 1 grain increased in children between eight and thirteen years by $\frac{1}{4}$ grain daily to a maximum dose of $2\frac{1}{4}$ grains, and in the

case of those aged fourteen to twenty years increased daily by $\frac{1}{2}$ grain to a maximum of $2\frac{1}{2}$ grains!

Furthermore, the total given to all children was 25-30 grains! Is it to be wondered at that in six children the treatment had to be stopped owing to unfavourable symptoms, or that toxic symptoms, such as coughing, vomiting, abdominal pain, evanescent rash, toothache, and gingivitis were noticed in the majority?

The reason given for the "relative severity" of those toxic symptoms, namely that so many of the children were suffering from malnutrition and cachexia, is obviously not correct - in Egypt the type of person most infected is the fellaheen, the poverty stricken agricultural labourers, who are generally affected by other debilitating parasitic disease such as ankylostomiasis and ascariasis ¹²³⁾ and from the Anthelminthic Hospitals it is reported ¹⁵⁵⁾ that coughing occurs on an average in ten per cent of the cases, nausea in 1.6%, vomiting in 3.8%, whilst toothache and gingivitis are not mentioned at all, nor are these latter symptoms referred to by any writer on the toxic effect of antimony in the treatment of bilharzia.

It seems obvious that the malnutrition and cachexia of the children should have been made the excuse for commencing treatment with smaller doses and for a smaller total amount of antimony injected

in each case, rather than for the severe toxic symptoms subsequently. It might be argued that time was an essential factor at these camps, but the course lasted thirty-three days. The opinion is however, put forward that the same percentage of cures (92%) could have been attained with a total of 20 grains in eighteen smaller and less toxic doses.

That the severe reactions at these camps has not been forgotten is evidenced by the following abstract from the 1929 Circular on the Standard Treatment of Bilharzia, issued by the South African Public Health Department, "Especially weakly and anaemic children (even if they show no definite cardiac or renal disease) should preferably be excluded from "camps" where mass treatment is carried out, as they are likely to react strongly to treatment, and prejudice the main object of the camp, viz. propaganda."

But that the failure of strict adherence to the instructions of the manufacturers of drugs is a weakness at the camps is further illustrated by an extract from the Annual report of the Union of South Africa Health Department 1930, ¹⁰⁾ "At the suggestion of this Department the new drug, "Fousdin", was tried in the treatment of this disease, but the result has not been uniformly satisfactory. A further test, with closer adherence to the instructions issued by the manufacturers will be arranged." ²⁰²⁾ A further revelation is made by Orenstein

that in many cases nearly double the recommended dose of Fouadin was given. Experientia Docet!?

Toxic effects which were encountered.

Cough - this symptom was observed in about 50% of the cases treated. It varied in the individuals in that some had it after every injection whilst others only at times - the latter, particularly with the larger doses. In most cases where it occurred it was just a short single cough and occurred almost concurrently with the placing of a sterilised swab on to the site of injection after the operation. In the cases where it was noticed with the first few injections, it became customary expectantly to wait for it, as an added verification - in spite of all precautions and the absence of local pain - that the injection had been properly administered and thus giving a certain degree of assurance and satisfaction which suggested to the writer its comparability to the first cry of a newly delivered infant.

In one case only (Piet) was the cough of great severity. Here each injection, small or large was followed by a paroxysm of coughing - lasting about three minutes - which was only relieved by vomiting. The explanation was obviously his bronchial irritability as evidenced by his asthma. Nothing was done in the majority of cases to prevent or treat the cough except allowing the patient to rest.

Cawston recommends sips of cold water ⁵⁸⁾ and codein, but in Piet's severe attacks nothing tried was of any avail.

Nausea - this was not a marked feature; it occurred in a few cases, particularly with the first injection.

Vomiting - this symptom was present in the first few cases treated. When it was realised by the amount of material vomited - and at times by the inconvenience of a soiled couch and floor - that it would be advisable to have smaller amounts in the stomach, the patients were warned not to have a heavy meal for a few hours before presenting themselves. This measure proved very efficacious.

Three cases including Piet, vomited persistently after each injection. In his case the vomiting was obviously brought on by the severe paroxysms of coughing.

No case of persistent vomiting after the patient had left for home was encountered.

According to Khalil ¹⁵⁵⁾ vomiting occurs in Egypt in 3.8% of cases. He remarks that if vomiting persists for twenty-four hours, it is an indication of poisoning.

Giddiness - this was quite a common complaint. but only directly after the injection and momentarily.

Rheumatic muscular pains - was a symptom fairly

often complained of, especially after the administration of the bigger doses and towards the end of treatment.

Tingling sensation - one patient, Piet, complained of a tingling sensation up the arm and down the body "na die toone toe" (down to the toes) "It is not unpleasant," he said, "and shows that the injection is travelling all over the body, and would thus do good." Whether this sensation was of psychological origin, or not, is impossible to say. No mention is made of any such symptom in the literature.

Herpes - the case just mentioned (Piet) provided the only example of herpes labialis; this also occurred towards the end of the treatment, when the larger doses were given. Khalil ¹⁵⁵⁾ refers to this complication, and says that it is usually accompanied by a temperature. In the case of Piet there was no pyrexia, and the condition cleared up soon after the final injection.

Other symptoms which have been recorded, after antimony tartrate injections but which were not encountered, are -

Catarrhal symptoms - Cawston in 1923 ¹⁵⁵⁾ reported that he was accidentally infected with bilharzia. During treatment with tartar emetic there were no untoward effects beyond catarrhal symptoms after the first few injections. These

symptoms, he suggests, may account for the many instances in which the injections are discontinued on account of "influenza" supervening. When Le Roux¹⁶⁶⁾ in 1929 pointed out that the worms in sheep infected with *S. mattheei* migrated to the pulmonary vessels on the injection of antimony tartrate, Cawston ventured the theory that this might be the explanation of the catarrhal symptoms during treatment. It might as well be put forward that this, too, is the explanation of the cough, but cough occurs when antimony is injected for conditions other than bilharzia.

Metallic taste in the mouth - Khalil¹⁵⁵⁾ reports this as occurring in some patients, but requiring no treatment.

Urticaria, itching and oedema - are reported by Lampe in 1926,¹⁵⁹⁾ who ascribes these symptoms to an anaphylactic phenomenon produced by the death of the parasites.

Dermatitis - with persistent itching sensation, and jaundice are reported from a few cases in Egypt.¹⁵⁵⁾

Otorrhoea, conjunctivitis and blepharitis - are described as occurring by Harsmat in 1921.¹³⁵⁾

Hack,¹²⁸⁾ of Pietersburg, Transvaal, in 1931 reports a case in which 20 grs. were given in about sixteen days to a European boy of fifteen. Nineteen days after the last injection he became pyrexial with cough, tenderness and resistance in the right hypo-

chondrium, epistaxis, delirium, sallow complexion impaired air entry at the right base, albuminuria and a temperature up to 106°F. It is particularly pointed out that the potassium salt was used.

Rise of temperature - in Egypt ¹⁵⁵⁾ it is found that this may happen on the day following the injection for any of the following reasons:-

- (a) Lack of proper sterilisation of the solution
- (b) The presence of a precipitate in the solution due to the use of stored distilled water, or to the decomposition of the drug.
- (c) The presence of impurities in Tartar Emetic, notably lead and arsenic. "The patient must not receive any injections as long as his temperature is above normal, whatever may be the cause. Grave toxic symptoms and even death may result from neglecting this precaution.

Toothache and Gingivitis - have already been remarked on as having occurred in the camp at Rustenburg

Collapse - is stated to be rare. ¹⁵⁵⁾ "It generally disappears very quickly It may be caused by injecting the fluid quickly or at a high temperature."

Sudden death - quoting from Khalil; ¹⁵⁵⁾ "It rarely occurs before the 6th injection and does not happen immediately after the injection, but usually after a few hours' interval. It often follows a strenuous muscular effort on the part of the patient when his body is fairly saturated with tartar emetic.

The drug exerts a toxic effect on the heart muscle. It is notable that the stronger patients are more liable to sudden death than the weaker ones. The death therefore astounds the relatives as well as the treating medical man. It is probable that the stronger patients are more liable to exert themselves physically It is the duty of the treating practitioner to warn his patients to abstain from doing their usual manual work during the treatment and for about one week after it There is no doubt that many cases are concealed by the relatives to avoid post mortem examination and legal enquiry. The real death rate may be about 0.5% per 1,000 cases of those that finish the course of treatment.

Fortunately one was spared this grave complication. It must be admitted that except for the half hour that the patient was rested after each injection no special precautions were taken, nor were the patients particularly warned against exerting themselves. Where haematuria was present they were advised not to run about, as a precaution against exacerbations of the bleeding.

EFFECT OF TREATMENT

On the Ova.

The ova, from being clear, translucent and yellowish, become granular, acquire a brownish

colour, later become still browner, and ultimately black. Their shape alters simultaneously with these changes, some appearing smaller and shrunken. Ultimately, in favourable cases, all ova disappear.

These changes occur at varying periods after the commencement of treatment depending, when present, on the dose of antimony tartrate used and the frequency of the injections. The urine was examined microscopically three or four times during the course of treatment and the alterations in colour were first noticeable during the second week. Towards the end of the 3rd week or during the 4th week all the ova in the urine were black.

Christopherson ⁸¹⁾ says: "It will be found that for a few days after the injection has been commenced, the ova are normal looking, alive, and behave like bilharzia ova are expected to do, but a time comes when some do not hatch, and later (it may be about 14-18 days) after the injections were commenced, (after about grains 20 were injected) when, although showers of ova occur in the urine almost daily, all are dead."

Changes in the ova in the cases treated in Egypt are stated to be noticeable after the 5th injection - the stages are the same as noted, but further diagnosis of death is made by impossibility of distinguishing the cephalic glands of the embryo and the absence of movement in the flame cells. ¹⁵⁵⁾

These minute details were never noticed.

Cawston ⁴⁸⁾ records that degenerating miracidia may be seen within the shells of the eggs shortly after the dose administered has reached a full grain, and that blackened ova may appear after a total of only $1\frac{1}{4}$ grains has been given.

Effect on the Patient.

It has already been remarked that the effect of treatment on haematuria is at times dramatic. Almost immediately after the commencement of treatment - at the 3rd or 4th injection, the blood passed was found to decrease in amount, and during the second week, as a rule, it entirely disappeared. In some cases it was noticed that the blood which had entirely disappeared was replaced by the lump of jelly already referred to in discussing the symptoms. The question put to the patient, instead of being "No more blood?" was altered to "No more jelly?" At this stage it was deemed advisable to warn the patient and the parents of the danger of stopping treatment, although the major symptom had been removed.

The general well being of the patient was remarkably influenced. From a psychological point of view the fact of bleeding having ceased had a marked effect on those who were aware of the seriousness of the symptom. The physical improvement can be summed

up in the words of the Director of Education for the Transvaal: ⁴⁾ "We have repeatedly seen puny, pale, underfed, tired retarded children become hefty, healthy and capable of competing with the best of their class within six months after they had been cured of the bilharzia."

Mentally the two cases who were behind in their class at school showed very slight obvious improvement in this respect, but from the mothers it was gathered that the changes in them were much more than were apparent to the observer.

In the case of Piet the asthmatic attacks, though aggravated after each individual injection at first, gradually became more infrequent and less severe. When seen three months later he admitted that he had not experienced any attack since the treatment had ceased.

The tired look of many of the boys was noticed to change to a bright expression. The complexions of the pale, sallow-faced boys were hardly affected by the treatment, but the case of Mrs. P.O. was dramatic. The erstwhile semblance to pernicious anaemia faded like magic. As the symptoms disappeared so rapidly and the anaemia was so obviously restored no blood counts were made. Within the first week the difference in her appearance was noticed; in the second week she was walking about, whereas

previously she had been practically bedridden for about two months. After the fourth week she walked out of the Hospital into which she had been carried.

DIAGNOSIS OF A CURE.

The greatest controversy exists as to the definition of a cure in Schistosomiasis. In endemic areas the difficulty of estimating a cure is increased by the easy opportunities afforded for reinfection.

Khalil ¹⁵⁵⁾ says that if the ova re-appear within two months after treatment, it is probably a true relapse, as two months are necessary for the maturation of a newly introduced parasite. That relapses can and do occur is evidenced by the following references.

Christopherson states that very occasionally after even a year, a case may commence to pass some more live ova, ⁸⁴⁾ and Khalil ¹⁵⁵⁾ records that in 14 children, in a waifs' home in Cairo, who had undergone a course of treatment, re-examination a year later showed relapses in 4, without any possibility of re-infection.

One has, moreover, to discriminate from a false relapse - the type of case that has already been described as chronic Schistosomiasis without living ova. The presence of ova in the urine does not

necessarily mean that the case is not cured.

Christopherson says: ⁸¹⁾ "For a considerable period (4 or more months) after the presumed death of the parent worms, ova are passed which have been deposited in the tissues before the death of the worms. These residual ova die in the bladder or rectal tissues in time, either naturally or killed by the antimony tartrate, and though dead they will find their way through the mucous membrane of the bladder or rectum. Therefore the presence of ova in the urine is no criterion that the parent worms are not dead, or that a cure has not been effected." He adds that in the process of "coming through" the tissues some red blood corpuscles may be caused to appear in the urine.

The period after which it can definitely be said that the patient is cured is, judging by the diversity of opinion, unsettled. ⁸⁴⁾ Christopherson is of opinion that "a case may reasonably be considered cured if after 365 days after injections have been completed there are no symptoms of the disease - no ova, no blood in the urine - after several examinations have been made at intervals."

Six weeks' freedom from ova is stated by Cawston to be the period after which a cure can be pronounced. ⁶⁴⁾ Phease ²⁰⁶⁾ takes the period in which the patient should be kept under observation as two years.

Apart from the re-examination of excreta for living ova there is at the present time no method of examination which can assure that all the schistosoma have been killed by the treatment adopted. Various means have been suggested with hopes of fulfilling these requirements. Fairly in 1927¹⁰⁸⁾ devised a complement fixation test for bilharzia, but of this one may say that, firstly, it is entirely a laboratory test; secondly, the material necessary for its performance is not always available; and lastly, that it is not claimed to be anything but of diagnostic value.

e/

Tells if worm is living

e/

Fairly and Hamilton¹⁰⁹⁾ (1927) originated an intradermal test, but this evidently is also limited - it is of diagnostic value only, and does not afford an indication of the success of treatment. In 1929 Tsykales and Riegl²⁵⁰⁾ advised, for making evident a latent schistosoma infection, the injection of gr. $\frac{3}{4}$ to gr. $1\frac{1}{2}$ of emetine and 4-6 hours later looking for, the appearance of blood and ova in the urine, where none were detected previously. No further work on this is traceable. In 1931 Macial¹⁷⁶⁾ reporting on the use of fouadin, remarks that when the compound is injected, there is a rapid increase in eosinophilia and this did not occur in persons uninfected with schistosomiasis. He does not, however, suggest this as of diagnostic importance.

Until a discovery of this nature is made - and

it should preferably be an easy and quick test capable of application in the consulting room - the only means at our disposal is repeated re-examinations of the excreta for live ova. In the cases here reported the patients were asked to present themselves for re-examination in three months' time, but only three did as requested. In these no ova were found. In the others, of whom sight was not lost, all stated that there was no return of the symptoms.

It is, therefore, not claimed that all the cases recorded have been followed up - from observations made during the treatment, subsequent enquiry, and in three cases from further examinations, it can be inferred that cures were effected in all the cases except the three who voluntarily discontinued the treatment.

CHAPTER VI.

THE PREVENTION OF SCHISTOSOMIASIS IN SOUTH AFRICA.

CHAPTER VI.THE PREVENTION OF SCHISTOSOMIASIS IN S. AFRICA.

The foundations of all rational schemes for the eradication of Schistosomiasis date from the time of the elucidation of its etiology by Leiper. They are similar in most countries and comprise four pillars on which the principles of all measures rest namely:

1. Destruction of the adult parasite.
2. Prevention of the Miracidia from reaching the water.
3. Eradication of the intermediate hosts.
4. Prevention of the cercaria from reaching its host.

Leiper's original recommendations were multiple and varied and applied particularly to Egypt. Some of those found effective have been adopted in other countries as a nucleus in their campaigns against the disease. Authorities on the subject have, since Leiper's work, added to the list and the total number of preventive measures suggested is formidable.

In the attempts at a successful issue in each and all of these problems, in S. Africa numerous details still need to be investigated. The Union

with the multiplicity of its local problems combined with the fact that it is only recently awakening to the dangers of this scourge forms a field where wonderful improvements could and should be made.

THE DESTRUCTION OF THE ADULT PARASITE.

The measure adopted in South Africa in this direction was the establishment in 1926 of "treatment camps" for scholars. This attempt at mass treatment on a small scale was sponsored by the Transvaal Education Department and took place in the worst of the endemic areas. In 1929 the Transvaal Education Department, the Transvaal branch of the South African Red Cross Society and the Union Public Health Department combined to form the "Transvaal Bilharzia Committee" which body was to foster "educative and publicity work in connection with the disease, advise as to preventive and precautionary measures and organise special 'camps' for mass treatment of affected scholars from time to time at various suitable centres." 9)

That the Union Health Department, in its first attempt at enthusiasm in 1926, considered mass treatment as an absolute essential in dealing with Bilharzia, is evidenced by the reference in its yearly report 6) to "voluntary or compulsory 'mass treatment' of sufferers." Owing, perhaps, to the paucity in numbers of those treated at these "camps",

it was realised that their main value lay in propaganda: "especially weakly and anaemic children should preferably be excluded from 'camps' where mass treatment is carried out, as they are likely to react strongly to treatment and prejudice the main object of the camp, viz. propaganda." 9)

In Egypt there are special Anthelmintic Hospitals for the mass treatment for cases of parasitic infestation. In 1920 there were 4 such hospitals with 3,609 new cases but so effective was the campaign against the disease that in 1928 there were 324,500 new cases with an increase of 44 hospitals. 155) In addition there were mobile hospital units which toured the villages to administer treatment to the inhabitants. In South Africa, however, such methods are not feasible. The country is too sparsely inhabited, the villages too scattered and their populations are too small to warrant the adoption of such measures.

In the South African attempts at "mass treatment" on a small scale can be seen the influence of the Egyptian plan of destroying the parasite in the human carriers as expounded by Christopherson. In his presidential address at the Royal Society of Medicine in 1928, 188) he pointed out that Khalil had estimated, that in Egypt almost half a million people a year presented themselves for treatment for Bilharzia; that antimony tartrate is cheap and cures 100%; that the Egyptian fellaheen does not

object to injections, and that by the establishment of mobile hospitals bringing the treatment to the villages, a substantial step would be made towards eliminating Bilharzia from Egypt.

In a consideration of his doctrine of, as it were, "no infected humans - therefore no infected snails", his comment on learning of the establishment of a "camp" in the Western Transvaal is instructive: ⁸⁷⁾ "With the school children cured and instructed in the knowledge of sanitation, the necessity for extermination of the water snail will not be so necessary because there will be few patients to infect the snail."

This attitude is deftly summed up by R.T. ²⁴⁵⁾ Leiper in the Tropical Diseases Bulletin:

"It is evident that the author's sympathies lie with the alternative method of irrigating the human veins with tartar emetic, in place of irrigating the water ways with copper sulphate."

Assuming a 100% cure, it is still obvious that the method of only irrigating the veins, cannot possibly be a major factor. To presume any measure of success from this procedure one has to take for granted,

- (1) that all infected persons will be cured;
- (2) that human beings would avoid infection by denying themselves the pleasures derived from bathing, fishing, wading and shooting in South Africa; or

that an only method of earning one's living, in which contact with water is essential, as in the case of the fellaheen in Egypt, could be refrained from.

But little consideration is needed to realise that concentration on this line of attack is not a criterion in the question of elimination. By all means cure as many as possible, of those infected, but rely more on the other direct and indirect benefits accruing from this method - the effect on the physical and mental capacity of these treated, the propaganda effect - rather than upon its influence on the water-snail as a disseminator of Bilharzia.

PREVENTION OF THE MIRACIDIA FROM REACHING
THE WATER.

Blacklock in 1925 remarked that endemic schistosomiasis is a sign of inadequate education in hygienic principles. ²⁶⁾ It is a matter of regret that this statement is verified by conditions in South Africa.

194)

The Medical Officer of Health for Pretoria, in his report for the year 1928-1929 quotes, from a newspaper, a description of the town twenty years previous: "Dirty water spruits (furrows) and accumulations of rubbish streets are used for depositing kitchen refuse, slops, empty tins and broken glass ... carcasses, rubbish

and filth are deposited on the outskirts of the town The water supply is putrid .. wells are in close proximity to cesspools and cesspools are overflowing into furrows the centre square of the town is used as a cattle-kraal and is bedecked with soil, chiefly animal excreta."

This description recalls to mind certain villages, visited not long ago, and, no doubt, many more could be found to fit the picture. The sanitary arrangements leave a good deal to be desired; the "pail system," combined with efforts of economy in service and the carelessness of the native labourers, produce a state of affairs that is anything but hygienic or aesthetic.

The mentality of the "poor white" has been referred to, but as far as it affects the disposal of his excreta it is unfathomable. In times of emergency the most staid and sedate are compelled to adopt unconventional methods, but, it would appear, that among the "poor whites" of South Africa, no such excuse is necessary.

Christopherson has said: ⁸⁸⁾ "The natives inhabiting tropical countries take medicines very well, but they take hygiene very badly." This is true, for the "blacks" of South Africa, particularly for those who inhabit the "locations" (separate districts set aside for natives only). These "locations", as a rule, have a "spruit" or two

running through them, and a good deal of laundering is done in this water, a fact which recalls to mind the incidence of bilharzia amongst washer-women in Portugal. ²²⁾

The solution to this particular aspect of the problem is a very difficult one. Various steps have been taken in different countries: Pit latrines were installed in the Hiroschima Prefecture ²⁴²⁾ in Japan, streams were put out of bounds in Sierra Leone, ²³²⁾ but, the only logical solution lies in the instilling into the mentality of the infected classes, the principles of hygiene - a colossal work in which publicity and propagands, as is being attempted in South Africa and Egypt, plays the most important role.

ERADICATION OF THE INTERMEDIATE HOSTS.

This, it seems, should be the major factor in dealing with the prevention of Bilharzia. If it were possible to achieve this, Christopherson's dogma of no infected humans - therefore no infected snails would be reversed: no infected snails - therefore no infected humans.

Before any attempt to eradicate the intermediate host is made, certain investigations have still to be undertaken in the Union. These are:

(1) the establishment of all the species responsible for the transmission of bilharzia, and

(2) a survey of the distribution of the snails concerned.

The keeping of domesticated ducks, and the prevention of the destruction of wild fowl, figure through South African literature as methods of diminishing the number of snails. Le Roux ¹⁶⁶⁾ points out, however, that there are hardly any experiments on record, which prove the use of the duck, as a means of controlling the increase of molluscs, and, that, his personal experience is, that *Lymnaea natalensis* may flourish in the pools frequented daily by water fowl. Predatory fish, such as trout, which feed on snails has also been recommended for the stocking of streams.

In 1928 Cawston ⁶⁵⁾ reported a fact of local interest. He writes: "The crushed root of *Tephrosia*, the common wild pea which the South African natives use to poison fish they wish to catch for eating, is very lethal (if undried or boiled) to *Physopsis africana*, because this species of fresh water snail does not crawl out of water so often as do other species. It is perhaps 100 times as useful as copper sulphate, as a means ready to hand, for destroying the *Bilharzia* snail host in South Africa, for 1 part in 25,000,000 is said to destroy fish within an hour without being poisonous to man or cattle." No reference to attempts to

utilize this discovery has been found.

The literature is not lacking in the number of chemicals, which have been stated to be lethal to the fresh water molluscs, and the uses of which are advised. Leiper in 1915¹⁶⁴⁾ suggested ammonium sulphate. Cawston in 1919⁴⁵⁾ mentioned Ross's Larvicide. Chandler in 1920⁷⁶⁾ recommended copper sulphate and Khalil¹⁵⁰⁾ in 1927 dramatically proved its efficacy in one of the villages in the Oasis of Dakla, where 63.5% were infected with *Schistosoma haematobia*. The main stream of the village was of artesian origin and was found to contain large numbers of *Bullinus* snails. The addition of copper sulphate, continuously for four days and four nights, resulted in the death of the *Bullinus*; when revisiting the area six months later, no living *Bullinus* was found. Khalil records this as "The Eradication of Bilharziasis: a Successful Attempt in an Endemic Area."

The dilution of copper sulphate originally advised by Chandler was from 1 in 500,000 to 1 in 2,000,000; Leiper, however, in 1922, found that 1 in 5,000,000 kills *Bullinus contortus* and *Planorbis boissyi*, while *Limnaea truncatula* required a dilution¹⁶⁶⁾ of 1 in 2,000,000. Le Roux, in South Africa, tried copper sulphate in a dilution of about 1 in 2,000,000 on *Physopsis africana* var *globosa* in a

pool and killed them all in 18 hours. He adds that as in the Transvaal, the collections of water, where Physopsis abounds, is lowest in winter, the non-raining season, this is the best time to select for an attack on the snails.

Ibrahim ¹⁴²⁾ considers the use of copper sulphate, for the control of bulinus, on a large scale, in the Nile Valley to be impracticable, although the method would be of great use in dealing with rice fields and small canals. His suggestion is that, Egypt being divided into four districts for purposes of irrigation, on each consecutive year irrigation should be completely stopped in one of the four divisions; during the three summer months - the Department of Public Health to concentrate, on that area, all their activities for treatment and prevention.

This mode of killing snails by drying was originally suggested by Leiper in 1915 ¹⁶⁴⁾, Le Roux, in 1929, points out that although "this method of killing snails may be practical in the irrigation canals in Egypt, it cannot be utilised in the Schistosoma infected areas of the Union." It is obvious from this statement that Le Roux has entirely brushed aside the serious question of the Irrigation schemes in South Africa. In illustration of the importance of this question the role that

the Nile, plays in the spread of bilharzia may be considered.

The conclusions arrived at by Leiper in 1915¹⁶⁴⁾ that the Nile can and does spread the snails coincide with those of Khalil³⁰⁷⁾. During the spring months of the year, the sluice gates are open and the Nile water is coursing through the canals of Lower Egypt, bearing with it large masses of fresh water weed and vegetation, and it is to this that most of the infested snails can be found clinging. Leiper further pointed out that one questionable point was whether it is not possible for the snails of the dangerous species to pass upstream from the small canals at certain seasons, as indeed other species of snails are known to do.

The importance to South Africa of these facts is acute - there is no equivalent to the Nile, but of irrigation schemes there are many - in 1930 in the report of the Director of Irrigation for the Union of South Africa³⁾ it is stated that there are 125 irrigation districts in the country. Haslam's findings in his report to the Empire Marketing Board in London in May, 1929,¹³⁶⁾ that the distribution of *Bulinus* coincided with the distribution of the irrigation schemes emphasise the potential danger of these canals acting as a highway for infected snails - whether they pass up or down

stream or in both directions. In the Report, he demonstrates by a series of maps, that "nearly everywhere, that an irrigation project is likely, one or other or both of these diseases (malaria and schistosomiasis) both closely associated with water channels, is waiting on the threshold." ¹³⁶⁾

In 1926 Cawston ⁶²⁾ sounded a note of warning in his expression of regret at the construction of a large dam by the Government at Hartebeestpoort without utilizing any methods of keeping the molluscan hosts under control. This dam, has been definitely proved to be inhabited by *Physopsis africana*; ⁶²⁾ it supplies the farms with water for many miles around and no doubt plays an important part in the increased incidence of *Bilharzia* in the Northern Transvaal. This contention is further borne out by an abstract from the Annual Report of the Union of South Africa Public Health Department in 1928: ⁸⁾ "There is reason to believe that in many districts of the Transvaal the prevalence of the disease has greatly increased during the last four years," that is, since the construction of Hartebeestpoort Dam.

Unfortunately the climatic condition of the country, with its long continued droughts, demands such storage of water. Nevertheless an attempt

should be made to survey the irrigation districts with this danger in view, and steps corresponding to the findings, should be taken for the eradication of the intermediate hosts. It may yet be proved, that in South Africa the irrigation of the canals with copper sulphate will accomplish more in the prevention of Bilharzia, than the irrigation of the veins with antimony.

PREVENTION OF THE CERCARIA FROM REACHING ITS HOST.

From the point of view of interpreting this statement literally, it is interesting to note that Narabayashi ¹⁹⁶⁾ in 1916, showed that a coating of oil on the surface of the water proved impervious to the cercariae. Among the native tribes in South Africa, certain are known for their partiality to besmear the whole body with oil or grease, and it would be interesting to discover the incidence of Bilharzia amongst them.

¹⁶⁴⁾ According to Leiper the cercariae can survive for only 48 hours. In the Union, where water from pools is utilised very frequently for domestic purposes, being, in many cases pumped into tanks, it is thus essential to store the supplies for at least two days before use - whether the water be used for bathing or for drinking. Infection through the mucous membrane of the mouth being a proved and accepted fact, it is interesting to note

that even on the state owned South African Railways the drinking water is not entirely free from blame in the spread of water-borne diseases. The following is taken from the Annual Report of the South Africa Health Department 1929: ⁹⁾ "Complaints have at various times been received of persons developing typhoid fever and other water-borne diseases, shortly after completing railway journies, during which water was drunk on the train. The Department has now inaugurated a system of supervision of railway water supplies. Assistant Health Officers include in their inspection duties the source and nature of such supplies."

It has been suggested in South Africa that the introduction of "millions" or "kurper" or other surface -feeding fresh-water fish into pools or streams may be a useful measure for destroying the cercariae.

To obviate the danger of eating infected watercress and other water vegetables it is advised that they be washed in salt water followed by rinsing in fresh water before being eaten.

The essential element, however, in the prophylaxis of Bilharziasis is to prevent the human host from reaching the cercariae, and this in South Africa is a very difficult task. Many a village in the Union has its favourite picnic spot and bathing

pool or dam. The prevention of infection in this, the major source of the prevalence of Bilharzia in South Africa, resolves itself into making these bathing pools safe - and this is a difficult task - or the provision of public swimming baths. Where these exist, at present, many of them are of water from the spruits and are therefore no improvement on the bathing pools, which the youngsters know are dangerous, and which, with the increase in propaganda, they might possibly avoid. The public swimming baths should be free to all, and measures should be taken to prevent mollusca from contaminating the water. This is a feature of the work of the Transvaal Bilharzia Committee.

Its activities, if persisted in, will take no mean part in the decrease, and, perhaps, eradication of "Rooi water" in South Africa. They have definitely established the dangerous spruits in certain areas, - for example in Pretoria, the details of which have already been quoted. They have "flooded the country with circulars" 166) erected warning notices at infected streams, persisted in the policy of publicity by the establishment of "camps" for mass treatment of school children, both white and black, given public lectures at which films showing the life cycle of the schistosoma have been exhibited.

That the medical practitioner should not be averse to adding to his knowledge of Bilharzia, has been touched upon throughout this paper. One further reference may be quoted. Le Roux of the Onderstepoort Government Veterinary Laboratory in 1929 writes: ¹⁶⁶⁾ "During a recent visit by some Northern Transvaal farmers to this Institution, it became evident that they know little about the cause and prevention of urinary Schistosomiasis. Most of them had never even seen the snail, responsible for the transmission of Schistosoma haematobia. Some of them questioned me for quite a time. One of the more elderly ultimately asked me, whether the medical practitioners did not know all about it, or if they did, why they did not tell them. Some of my experiences with medical practitioners, prove that the farmer had reason to ask that question.

²⁷⁾ Blacklock in 1931, in discussing the education of doctors, expressed the opinion, that the curriculum of the tropical schools is overcrowded: "our aim should be, that every one should be, as far as possible, absolutely sure of the diagnosis and treatment of the common serious tropical diseases and of the simplest, and most effective means of preventing such diseases " - a statement heartily endorsed.

The Transvaal Bilharzia Committee has invited

interested persons to send in snails for identification and reports. Unfortunately, in the spirit which pervades the Union concerning Bilharzia, the response was meagre - one snail in a year was sent. ⁹⁾ This indifferent attitude can, and would, be corrected, if the suggestion which is later made were carried out.

In general, the Transvaal Bilharzia Committee has shown an interest in the problem of Bilharzia, which somehow seems foreign to South Africa and which is, therefore, all the more praiseworthy. The idiom of Paul Kruger, "Alles zal reg Kom" (Everything will come right) has for too long, been the policy of the powers that be.

In a leading article on the Presidential Address delivered by Dr. Leith to the Congress of the Medical Association of South Africa in May 1929, we find: ¹⁴⁵⁾ "Dr. Leith urges us to take no delight in dallying. 'Let us hasten very slowly' is an old slogan with many of us; like the supposition that everything will ultimately right itself, it is a phrase that has been responsible for more calamities in South Africa, than those, with which nature, or the politicians, have supplied us. It is time we ignored it. Festination may be pathological, but only becomes so, when there is loss of central control. Dr. Leith's remarks should stimulate us all

to consider the matter from a new angle. Already we note signs of a willingness to express more than pious hopes and impossible expectations. We have had resolutions moved at the Public Health Section and opinions expressed at other sectional meetings ... that show that we are aware of how much behindhand we are in this country

In the spirit of co-operation, which the Transvaal Bilharzia Committee invites, the following suggestions are put forward:

1. That the resources of the South African Institute for Medical Research and of the Onderstepoort Veterinary Laboratory be combined for the investigation of:
 - (a) The exact species of water snails and of animals, which are intermediate hosts for the schistosoma in South Africa.
 - (b) The exact distribution of these species in South Africa.
 - (c) The establishment of the geographical distribution of Bilharzia in South Africa.
2. That the Medical Officers of Health, throughout the Union, be held responsible for the sending in of snails, for identification, and report of infestation, to the Institutes named - failing the presence of a Medical Officer of Health on the District Surgeon should fall "the" onus.
3. Municipalities or other local bodies should protect the public by:
 - (a) protecting their public domestic water supply by means of filtration or by storage for several days before distribution (ordinary chlorination treatment alone is insufficient).

- (b) Rendering infested swimming baths safe by screening the intake-pipes with gauze to exclude snails and treating the water with 1 part in 1,500,000 copper sulphate;
 - (c) clearing slow streams and pools of all vegetation in order to starve out the snails;
 - (d) placing warning notices near all infested or suspected streams or pools within their areas;
 - (e) arranging, where practicable, for curative treatment of active bilharzia patients in their areas;
 - (f) educative propaganda in all schools as well as among the general public (native as well as European) in their areas;
 - (g) preventing pollution of the soil and of all streams or pools within their areas with human excreta by means of warning notices as well as by the provision of suitable and sufficient latrines near bathing-pools and elsewhere where necessary in their areas.
4. That the children, who have been treated at the "camps", be re-examined at regular intervals by the Medical Inspector of Schools in the course of their periodic visits.
 5. That Rooi Water should be included in the list of notifiable Disease, for the Union of South Africa.

The adoption of these suggestions, it is felt, would enable our country to make up the leeway it has lost, particularly in reference to the eradication of the scourge of Bilharzia.

APPENDIX.

APPENDIXThe recently introduced complex organic
Antimony Compounds.

That Antimony is the drug which fulfils the role of an ideal specific cure for Bilharzia is undoubted. The aim, however, of all experimental work has been the preparation of an antimony compound which, compared with the tartaric acid salts, should have a greater margin of safety between its toxic effect on the schistosoma and on man; which should be as efficient if administered through other channels than directly into the blood; or if intravenous injection be unavoidable, should at least not have the ill effects consequent on accidental extravasation around the vein; and lastly, which should reduce the time taken for the effective destruction of the worms.

Egypt with its millions of infected people, with its ever-increasing number of Anthelmintic Hospitals, and with a personnel of practitioners who are keen on finding a solution to this immense problem, forms the most colossal laboratory for research work and there is no doubt, that there, it is, that advances are being, and will be made. The

most recent advance is the introduction of "Fouadin".

Khalil reports ¹⁵⁵⁾ : "In an attempt to develop the Antimony treatment, the example of arsenic was followed. The trivalent arsenical organic compound "Salvarsan" and the pentavalent "Atoxyl" and "Spirocid" manifested extraordinary specificity and lower toxicity in the treatment of several diseases. The first successful attempt to produce organic antimony compounds was made by Schmidt (1911)", but he gives no reference to this statement, nor can reference be found.

"Stibenyl" was the first organic compound that met with any measure of success in treatment. Ziemann ²⁵⁵⁾ and Schirokauer ²²⁶⁾ in 1925 were im-
pressed with its effects although Manson-Bahr ¹⁸³⁾ five years previously had found it inactive. Maciel ¹⁷⁷⁾ in 1928 found it inferior to tartar emetic and Staudt ²³⁸⁾ in 1930 reported it as ineffective.

"Stibosan" or "471" was the next pentavalent antimony compound tried. Here again Maciel ¹⁷⁸⁾ after trying it on four cases, concluded that it was inferior to tartar emetic, whilst Khalil ¹⁵⁵⁾ after exhibiting it in two cases, found that it had no advantage over, and that it had to be supplemented by, tartar emetic.

"Neostibosan", or "693B" also a pentavalent antimony compound, is claimed to be the least toxic of all organic antimony compounds. In 1931 Khalil ¹⁵⁵⁾ - who is the most prolific writer on

bilharzia - stated that it had not been tried in schistosomiasis; but in this he was not correct, as Staudt ²³⁸⁾ had already, in the previous year, reported that it was inactive.

The next preparation to be tried was Sb 212 (Bayer). The features of this compound as investigated in Egypt were: ¹⁵⁵⁾

(1) its marked diuretic effect;

(2) instability on keeping or when prepared in a more concentrated form. Its use was discontinued after a fatal issue in one case out of 191 although the report admits that in this case - a girl - more was given than her weight indicated. ¹⁶⁶⁾ Le Roux in South Africa used it on sheep without any marked success; the preparation however was old, and had been in store for two years.

Two other salts of antimony - Antimony Sodium Thioglycollate and Antimony Thioglycollamide, were also investigated. The use of these in the United States in the treatment of granuloma inguinale - with less toxic effects than Tartar Emetic - stimulated Shattuck and Willis ²³⁰⁾ in 1928 to a trial with markedly beneficial effect, in one case of urinary Schistosomiasis. In 1930 Shattuck ²³¹⁾ reported 14 cases of Schistosomiasis with prompt relief of symptoms from doses, small both individually and in total, but the paper is incomplete without adequate following up of the cases, a factor of much importance and which has already been discussed.

A great number of other complex compounds were experimented with. Most of them were discarded owing, either, to their toxicity not being less than Tartar Emetic, or, the method of application or the duration of treatment did not show any advantages over the latter. The stepping stone to the introduction of what Khalil ¹⁵⁵⁾ considers to be a preparation which gives better results than tartar emetic, namely, Fouadin, was the compound Antimosan, or Heyden 661.

Antimosan or Heyden 661, a complex antimony salt of pyrochatechin had the great advantage that it could be given intramuscularly, though preferably intravenously. Specht ²³⁶⁾ in 1926 in Germany, treated two Egyptian students with Heyden 661, and effected a rapid cure, without any unpleasant after-effects. Tootell ²⁴⁴⁾ in 1927 reported that it was less toxic and just as effective as Tartar Emetic. In South Africa Orenstein ²⁰⁰⁾ in 1928 and Cawston ⁶⁹⁾ in 1929 used it on two and one cases respectively, but both report more confidently on its non-toxicity than on its efficacy. Cawston ⁶⁹⁾ had to supplement it with Tartar Emetic. Amongst others who reported that it was preferable to Tartar Emetic and other antimony compounds were Rubitschung ²²¹⁾ and Maciel ¹⁷⁷⁾ in 1928. In Egypt two series of observations made on 55 and 64 cases respectively, treated with Antimosan intramuscularly, produced

the following conclusions: that it is as efficient in curing schistosomiasis as Tartar Emetic; it is relatively less toxic if laboratory animals are used; it is, however, not tolerated by a certain percentage of human cases; that it produces in about half the cases **bradycardia**, due probably to stimulation of the vagus. ¹⁵⁵⁾ In the series of 55 cases, one case died and two showed symptoms of intolerance.

With regard to the local reactions, the report states "the drug when injected intramuscularly was definitely painful" but "no induration, abscess or inflammation developed locally." The drug was then tried intravenously, but the conclusions arrived at were the same as that of Orenstein and Cawston. (vide supra).

New Antimosan I and New Antimosan II followed antimosan. The reactions were milder, especially as regards the local pain, but there were certain disadvantages which led Schmidt to produce a sodium instead of a potassium salt. This new compound after exhaustive experiments on animals in Cairo was employed in man. The dosage and duration of treatment was worked out. It was then named "Fouadin" and put on the market.

In July 19~~1~~9, Khalil and his co-workers, Nazmi Peter, El Din and El Batash, ¹⁵²⁾ reported the results of treatment with Fouadin of 300 Schistosomiasis cases. In a communication by Khalil

and Retache ¹⁵⁶⁾ in February 1930 on the treatment of 2041 cases and later in a statement by Khalil ¹⁵⁵⁾ in January 1931 wonderful claims as to its efficacy and superiority to tartar emetic were put forward.

It is advantageous to review briefly the methods employed and the results obtained in Egypt.

Fouadin is supplied in the form of sterilized 6.3% solution, in boxes containing a series of ampoules for the treatment of a single case. (For mass treatment 100 c.c. ampoules are also available) 0.0085 gram. of antimony is contained in 1 c.c. of solution.

Dosage.

After preliminary study the following doses were decided on for adults of normal weight:

1st day	1.5c.c.	of Fouadin	7%	solution	intramuscularly
2nd "	3.5c.c.	"	"	"	"
3rd "	5.0c.c.	"	"	"	"
5th "	5.0c.c.	"	"	"	"
7th "	5.0c.c.	"	"	"	"
9th "	5.0c.c.	"	"	"	"
11th "	5.0c.c.	"	"	"	"
13th "	5.0c.c.	"	"	"	"
15th "	5.0c.c.	"	"	"	"

Total 40.0c.c.

In the case of children or weak individuals the doses are given according to the body weight, as has been explained is the custom of Egypt with Tartar Emetic.

If living ova persist in the excreta after the 9th injection one or more doses are given. It is

very rare to need more than 11 injections of Fouadin to effect a cure. If ova still continue to appear after the last injection with the ordinary course, they very often disappear after an interval of a few days without any further treatment. This is explained as being due to the cumulative effect of the drug. Sometimes similar occurrences are noticed after the Tartar Emetic course, but it is much more frequent after Fouadin treatment.

Duration of Treatment.

The course of treatment extends over two weeks, as against 4 weeks needed for Tartar Emetic.

Site of Injection.

The drug can be injected intramuscularly with safety, and the site generally chosen is the gluteal muscles, using the two sides alternately. There is very slight pain, which lasts for a few seconds after the injection, and it is bearable even by young children without any complaint. The injections can be given also into the back of the arm. Tenderness lasts for a few days, but generally there is no inflammation.

Symptoms following Injection.

Cough does not occur after Fouadin. This characteristic gave it an advantage over Tartar Emetic in the treatment of Schistosomiasis cases suffering at the same time from pulmonary tuberculos-

is or other chronic lung complaints.

Nausea unaccompanied with vomiting was absent amongst the 2,000 cases treated.

Vomiting as a symptom was present in a few cases - actually in 0.36%. It generally occurs with the later injections, and if persistent may be taken as an indication of intolerance.

Dizziness was noted, but rarely (0.018%)

Abscess formation - two cases in about 20,000 injections.

Bradycardia occurred after Fouadin injections, but to a lesser extent than after Antisoman. The normal pulse rate may be reduced by more than 12 beats in a minute. "Although from clinical evidence it may appear that the slowing of the heart is due to the stimulation of the vagus, the pharmacological studies failed to establish such a phenomenon in animals so far it has not yet produced any definite effects."¹⁵⁵⁾

Death - 2 deaths occurred - one in 2,041 cases and the other later, but no statistics were given as to how many were being treated. One death occurred in the same manner as with Tartar Emetic - suddenly after muscular exertion.

Effect of Fouadin on the Ova.

The change resembles in detail those seen in Tartar Emetic treatment, and rarely appears before

the 4th injection. "The condition of the ova when the patient is discharged as cured varies. There must be no living ova in the excreta, but granular or shrunken ova or a mixture of both may be present, or ova may be totally absent." ¹⁵⁵⁾

The Immediate Result of the Treatment.

"The result of the Fouadin treatment is equal to, if not better than, that of the Tartar Emetic treatment. During 1929 Fouadin was employed as a routine out-patient treatment in the Cairo Anthelmintic Hospital for a period of 5 months. The total number treated up to the end of 1929 was 2,041. The total cured (cases with no living ova in their excreta at the end of the treatment) was 61.4%."

Comparison of the Results of Fouadin Treatment with those of Tartar Emetic Treatment.

Arrangements were made to treat cases on alternate days by the two methods at the same hospital. A short abstract of the results obtained is here appended.

	<u>Tartar Emetic</u>		<u>Fouadin</u>	
	<u>No.</u>	<u>%</u>	<u>No.</u>	<u>%</u>
No. of cases	1000		1000	
Total cured	432	43.2	686	68.6
Did not complete the treatment, by ab-				
senting themselves	501	50.1	260	26.0
Refused the treatment	176	14.9	128	11.3
Total cases completed the course	499		740	
Total cured	432	86.6	686	92.7

It is evident from the above table that Fouadin gave better results.

(a) The duration of treatment is 10 days less than that of Tartar Emetic. The importance of this to a poor population, depending upon daily employment for their living, cannot be over-estimated. This is probably the most important reason for the greater percentage of patients who did not complete the Tartar Emetic course (50.1%) as compared with that not completing the Fouadin course (26%).

(b) The treating capacity of the unit is increased by about one-third, representing the reduction of the daily attendance of the patients.

(c) The absence of local complications as a result of the injections. The occurrence of inflammation, abscess, or sloughing was an important factor in patients discontinuing the treatment, and in new cases being frightened to present themselves for examination and treatment.

(d) The higher percentage of cure with Fouadin is not so great as to be of value in preferring one treatment to the other.

The disadvantages of Fouadin treatment however are:

(a) Its expense. Tartar Emetic is a very cheap drug and its preparation for injection is very simple.

(b) The action on the heart causing bradycardia in certain cases. The significance of this bradycardia is not yet fully elucidated.

(c) Its being monopolised by one Company, to which is naturally left the duty of control and standardisation of the preparation.

Before discussing the value of this compound it is as well to investigate the results of other workers.

Gordon and Hicks ¹²⁶⁾ in October 1930 reported that of six severely infected children treated with Fouadin in the prescribed dose, five of them lost 1-3 lbs. in weight, and "in one instance a persistent vomiting lasting four days occurred, and it was not considered advisable to continue the course." Considerable local pain accompanied the bulky intramuscular injections.

Maciel ¹⁷⁶⁾ who experimented with Fouadin on animals, verified that the toxic dose was far higher than the therapeutic one. Disagreeing, however with Khalil and his co-workers, the author states that it has a toxic action on the liver and needs careful watching, but that as a rule it is well tolerated. Quoting Peter, he reports that 75 out of 80 patients were cured. Details are given of 7 cases, one of whom showed intolerance, vomiting and prostration. He further points out that there is a rapid increase of eosinophilia to 20% or more, but that this returns to normal usually within 60 days after the drug is stopped. In patients not infected with Schistosomiasis, the drug caused no rise in the

number of these corpuscles.

The experiences with Fouadin in South Africa are represented in the records published by Cawston, Orenstein and the Union Public Health Department.

In June, 1930, the Annual Report of the Union of South Africa Health Department ¹⁰⁾ reads:

"At the suggestion of this Department, the new drug "Fouadin" was tried in the treatment of this disease (Bilharzia), but the result has not been uniformly satisfactory. A further test, with closer adherence to the instructions issued by the manufacturers, will be arranged. Antimony Tartrate still remains the most effective as well as the cheapest drug for treating the disease, but the introduction of a cheap and effective remedy which would be more easily administered and never give rise to any ill effects would be a notable advance."

In July 1930 Cawston recorded two cases where fouadin produced late vomiting and gastric disturbances. In one the drug had to be discontinued after the 3rd dose and in the other 53.5 c.c. were given in 31 days. Normal ova of Schistosoma haematobium were present in the urine three months later, and it was frequently bloody. ⁷²⁾

In November 1930 the same practitioner wrote: ⁷⁴⁾
 "Fouadin was widely advertised It was claimed that the drug was free from undesirable toxic

effects The claim was even published that three injections might effect a cure. Indications of severe hepatitis following the use of fouadin, even where there was no question as to the stability of the supply, were allowed to pass unheeded Due consideration of the pathological condition of the patient forces one to the conclusion that the use of fouadin in these patients frequently results in severe hepatitis, a complication which is greatly to be feared in persons whose liver function is already impaired through the presence of schistosoma invasion."

The communication brought a vehement reply from Orenstein ²⁰²⁾ in January 1931. As the one who drew the attention of the South Africa practitioners to fouadin, and as a member of the Transvaal Bilharzia Committee, he asked Cawston to substantiate his statement that the drug frequently causes severe hepatitis, to give a detailed description of the pathological condition of these patients, and to state his reasons for concluding that fouadin is more deleterious than tartar emetic. The last portion of the defence is so interesting that it warrants quoting in full:

"The rest of his (Cawston's) contribution seems to me, more or less, beside the point except the innuendo that cases of severe hepatitis occurred and were deliberately kept from public knowledge. This can only refer to the work of the

Transvaal Bilharzia Committee, as indeed Dr. Cawston made some such statement to me in a private letter. He also in this letter stated 'that he was given to understand that one death occurred in a child who had received fouadin.'

"The facts are that the child in question died of the sequelae of measles, had no fouadin, but two injections of tartar emetic. Fifty cases were treated with fouadin in the 'camp', which seems to prey on Dr. Cawston's mind. In many cases nearly double the recommended dose of fouadin was given, and the administration was venous and daily. Not a single case of permanent damage to the liver was observed the only ill effects observed referring to the liver were tenderness and enlargement in a few cases."

"In conclusion may I say that although I am not prepared to advocate the complete substitution of fouadin for other drugs in the therapy of schistosomiasis I feel that fouadin is a valuable addition to our armamentarium, possessing special advantages under certain circumstances, such as treatment of ambulatory cases in young children, and that its dangers - when properly used - are not greater than those associated with tartar emetic."

The official statement issued by the Public Health Department in June 1931 reads ¹¹⁾ : "At one camp 50% of the children were treated with fouadin, the remainder receiving the usual intra-

venous injection of tartar emetic solution. The medical officers in charge considered that fouadin treatment compared very favourably with the older method in regard to ease of administration, length of treatment, after-reaction and curative results. It is, however, a very expensive mode of treatment and it is essential that the drug be administered exactly as prescribed by the manufacturers."

Only one more recent reference about fouadin is found in the literature and is of great importance: Cawston ⁷³⁾ in October 1931 reports that in spite of jaundice and bile-stained urine he employed fouadin in a girl of 18 "in the usual doses", which he quotes as 1 c.c., 2 c.c., and then $2\frac{1}{2}$ c.c. consecutively - and that the end of treatment degenerating ova had completely disappeared, and in the next few weeks the patient gained 20 lbs. in weight!

To sum up, then, against fouadin, there are the few reports of toxic effects. In favour of it, Khalil states that fouadin gives better results than tartar emetic; Orenstein and the Public Health Department consider it as comparing very favourably, whilst Cawston - of whom Sharp ²²⁷⁾ in 1924 said: "No man in South Africa, has given more thought and energy to the study of this disease and with such success" - has evidently discovered that in an amended dosage, even the presence of jaundice before treatment does not lead to severe hepatitis. One cannot ignore the fact that in Egypt the compound

has had a severe test and has emerged triumphant. If subsequent trials produce similar results, a specific safe and easily administered remedy for Schistosomiasis will be in the hands of clinicians. A greater adjunct will be presented to aid in the eradication of Bilharzia.

SUMMARY.

- (1) In 1958, the ...
- (2) ...

SUMMARYCHAPTER I.THE HISTORY OF SCHISTOSOMIASIS.

- (1) Egypt has been infected with Schistosomiasis since time immemorial.
- (2) In 1851 Bilharz discovered the causal parasite.
- (3) In 1864 John Harley showed the variety of Schistosomiasis present in South Africa to be identical with that in Egypt.
- (4) Sambon adopted the name *Schistosoma mansoni* for a new species in 1907.
- (5) In 1915 Leiper worked out the life cycle and determined the intermediate hosts in Egypt.

CHAPTER II.THE INTERMEDIATE HOSTS OF SCHISTOSOMIASIS

- (1) In 1888 Allen in South Africa suggested that the infection was intimately associated with bathing.
- (2) Controversy ranged between Looss, Sir Patrick Manson, Wolff, Bour, Conor as to whether there was an intermediate host necessary and if so which stage in the development of the parasite infects man.

- (3) In 1913 Miyaira succeeded in infected animals with cercariae after failing with miracidiae.
- (4) Leiper in 1915 established that the mollusc intermediate hosts in Egypt are:
 For *Bilharzia haematobia*:- *Bulinus contortus*,
Bulinus dybowski,
Bulinus innesi.
- For *Bilharzia mansoni*:- *Planorbis boissyi*.
- (5) The first effort to determine the intermediate hosts in South Africa was by J.G. Becker in 1916. He established that *Physopsis africana* harboured *Bilharzia cercariae*.
- (6) In 1920 Porter identified *Lymnaea natalensis* as a carrier of *Schistosoma haematobium* and *Physopsis africana* and *Planorbis pfeifferi* as harbouring *Bilharzia mansoni*.
- (7) Cawston in 1921 found *Schistosoma bovis* in man and its larva in *Physopsis africana*.
- (8) *Physopsis conicum* implicated as a carrier of *Schistosoma haematobium* by Porter in 1925.
- (9) In 1925 Cawston recorded the presence of *Schistosoma spindalis* in a schoolboy.
- (10) Porter in 1926 reported two cases infected with *Schistosoma bovis* and announced that she was able to infect experimentally *Planorbis pfeifferi* and *Isidora tropica*.
- (11) Veglia and Le Roux discovered the presence of *Schistosoma mattheei* in sheep in the Eastern Cape Province.

- (12) In 1930 Porter reported the presence of *Schistosoma japonica* in a single specimen of *Lymnaea natalensis* .
- (13) There are many difficulties in estimating the snail distribution in South Africa.
- (14) South Africa is fortunate in having the Medical Research Institution and a Government Veterinary Research Laboratory at Onderstepoort. These should unite in such investigation.
- (15) A brief note is given on the bionomics of *Physopsis africana*, the common snail host in South Africa.

CHAPTER III.

THE INCIDENCE OF SCHISTOSOMIASIS IN S. AFRICA.

- (1) The difficulties in estimating the true incidence are due to:
 - (a) the mildness of the symptoms,
 - (b) the outlook of the "poor whites" towards Bilharzia,
 - (c) the impossibility of correctly estimating the incidence among the natives,
 - (d) Schistosomiasis not being a notifiable disease.
- (2) Incidence with regard to age.

85% of the cases observed were of school age. A similar age incidence is found in Natal and in the Transvaal.

The same age incidence was recorded by the earliest observers in South Africa.

In Egypt, Guinea, Palestine and other countries the same age incidence is found.

(3) Incidence with regard to sex.

In the group of cases analysed only one was female.

Other records in South Africa also point to the comparative rarity of the disease among the female sex.

Such distribution among the sexes is universal except in Tavira (Portugal) and Toma.

(4) Incidence with regard to race and religion.

Natives, Indians, and Europeans are all infected.

Religion is not a factor in South Africa as it is in Egypt, Palestine and other Mohammedan countries.

Allen suggests that circumcision among the Jews was carried out originally as a prophylaxis against Schistosomiasis.

(5) Incidence with regard to class.

- (a) Mostly schoolboys are affected.
- (b) "Poor whites" are particularly liable.
- (c) Troops as a class are subject to infection. This was well seen during the Boer War.

(6) Incidence with regard to geographical distribution.

Schistosomiasis is very widespread in the Union but appears to be localised to certain well-defined areas.

The distribution does not correspond with that recorded by Byam and Archibald.

In Natal it is present all along the coastal belt. Occasionally cases occur in the higher altitudes.

There is no *Bilharzia* in the Orange Free State.

The Cape Province is only infected in its Eastern half. There is no *Bilharzia* West of Knysna.

In the Transvaal the disease abounds in the North, the East, and the West, particularly the country supplied with water from the Hartebeespoort Dam. Many favourite picnic places are known to be infected.

(7) Incidence with regard to the type of Schistosome.

Schistosoma haematobium is most common.

Schistosoma mansoni.

Schistosoma bovis, or *S. mattheei vel bovis*.

Schistosoma spindalis, or *S. spindalis var. africana*.

Schistosoma japonica.

CHAPTER IV.THE SIGNS AND SYMPTOMS OF SCHISTOSOMIASIS IN S. AFRICA

- (1) The signs and symptoms in South Africa unlike those seen in Egypt, are mild.
- (2) The incubation period is estimated as 3-6 months.
- (3) Early signs and symptoms:

These are not usually seen. Itchiness of the skin followed by vague symptoms, malaise, pyrexia, and general mild gastro-intestinal symptoms are suggestive.

- (4) Symptoms and signs of established disease.
 - (a) Haematuria - is the most common and obvious sign but it may not be present.
 - (b) Pain - is not a common feature. It may be due to cystitis or renal colic.
 - (c) Frequency of micturition - is a symptom occasionally met with.
 - (d) Mucoid discharge from the urethra - was a very common symptom among the cases personally treated. This discharge often replaced the blood in the urine after treatment was commenced and was taken as an indication of improvement in the patient's condition. No reference to this as a symptom can be found in the literature reviewed.
 - (e) Backwardness at school - is very commonly a result of Bilharzial infection and the underlying cause is often overlooked.
 - (f) Anaemia - a case is recorded resembling Pernicious Anaemia in appearance.
 - (g) Appendicitis - is not uncommonly caused by *Schistosoma haematobium* in South Africa. Its correct aetiology can be diagnosed at operation from the appearance of the tissues.

- (5) The signs and symptoms of advanced disease are very rarely seen in South Africa.
- (6) Special signs and symptoms.
- (a) Affection of the female genital organs - is occasionally seen. A description of the lesions commonly found is given.
 - (b) Calculi - are rarely seen among the natives, but appear to be more common among the Europeans.
 - (c) Nervous Symptoms - mental retardation is common. Epileptic fits have been seen to clear up with treatment.
 - (d) Rectal symptoms - a case is recorded where *Schistosoma haematobium* was found in the faeces, but was causing no rectal symptoms. Such symptoms are apparently not common in South Africa though the occurrence of Bilharzial appendicitis is not rare.
 - (e) Pulmonary symptoms - bronchitis may be an early symptom. A case is recorded where Bilharzia was complicated by asthma and attacks of coughing. No ova were found in the sputum.
 - (f) Pigmentation of the face - was described by Sinderson in Bagdad but was not seen in South Africa.
- (7) The diagnosis depends on;
- (a) Microscopical examination of the urine for ova.
 - (b) Examination of the faeces for ova.
 - (c) Examination of the blood for the presence of eosinophilia.
 - (d) Cystoscopic examination is useful to an experienced operator.
 - (e) X-ray appearances are not diagnostic.

CHAPTER V.THE TREATMENT OF SCHISTOSOMIASIS.

- (1) The first attempt to kill the worm was made by Fouquet, thirty four years after Bilharz's discovery of the aetiology of Schistosomiasis, using Extract of Male Fern.
- (2) Perchloride of Mercury; Santonin intravenously; Electragol; Salvarsan; Quinine; Thymobenzol; Methylene blue; Mercurochrome; Calcium; and carbon tetrachloride, were various drugs used at different times.
- (3) Ionisation; X-rays; and Diathermy have also been tried.
- (4) ~~Emetine~~ was found of value and is still used in certain cases.
- (5) McDonagh in 1912 was the first to use tartar emetic in the treatment of Schistosomiasis.
- (6) It was Christopherson who first appreciated the value of tartar emetic in the treatment of bilharzia.
- (7) The use of Potassium Antimony Tartrate was advised by Cawston and Christopherson. In Egypt Sodium Antimony tartrate was replaced by the potassium salt.
The Public Health Department of S. Africa recommended Sodium Antimony Tartrate.

- (8) No description can be found in the literature, of the results obtained from treatment with Sodium Antimony tartrate.

The personal treatment of thirty four cases is described.

- (9) The results obtained were very good and were attributed to the following factors:
- (a) Choice of preparation.
 - (b) Preparation of the solution for injection.
 - (c) The freshness of the solution.
 - (d) The warmth of the solution.
 - (e) The technique of the injection.
The syringe and needles.
The position of the patient.
The tourniquet.
The injection.
 - (f) The correct estimation of dosage. A comparison is given between the dosage used and that recommended by the Union Public Health Department.
For adults: an initial dose of $\frac{1}{2}$ grain. A maximum of 2 grains, with a total of 20-25 grains.
For children: "The younger and more poorly nourished the child, the smaller the dose."
Smaller doses were given than were recommended by the Union Public Health Authorities.
 - (g) The duration of treatment.
Average was about one month. In the treatment Camps it was about six weeks. In Egypt treatment course lasts about four weeks.
 - (h) Realisation of the significance of contra-indications. The only real contra-indication is chronic Schistosomiasis with the presence of non-viable ova in the excretions. One, such case, was met with. As very little is known in South Africa concerning this condition current opinion is quoted fully.
Debility is merely an indication for a smaller dose. Heart disease and renal disease may be contra-indications.

- (10) The trauma of the injections caused local tenderness in some cases.
Necrosis and sloughing may be local complications of injection.
- (11) General toxic effects were frequently seen in the treatment camps in South Africa and were due to overdosage. The cachectic condition of the children was given as an excuse for this occurrence rather than an indication for the administration of smaller doses.
- (12) The toxic symptoms encountered were:
- Cough,
 - Nausea,
 - Vomiting,
 - Giddiness,
 - Rheumatic muscular pains,
 - Tingling sensations,
 - Herpes.
- (13) Toxic Symptoms described by others are:
- Catarrhal symptoms,
 - Metallic taste in the mouth,
 - Urticaria, itching, oedema,
 - Dermatitis,
 - Otorrhoea, conjunctivitis,
 - Blepharitis,
 - Rise in temperature,
 - Toothache and gingivitis
(only seen in the camps in
S. Africa).
 - Collapse,
 - Sudden death.
- (14) The effects of treatment.
- (a) The ova became granular, brownish, shrunken and black within four weeks and finally disappeared from the urine.
 - (b) The patient showed marked improvement in the symptoms. The haematuria cleared up rapidly. The Anaemia improved dramatically and the mentally backward children brightened up considerably.

- (15) The diagnosis of a cure is difficult to make. The complement fixation test, the intradermal test, and the giving of a provocative dose of emetine to precipitate ova in the urine are of no value. Repeated examinations of the excreta for living ova is the only reliable guide.

CHAPTER VI.

THE PREVENTION OF SCHISTOSOMIASIS IN S. AFRICA.

- (1) The principles of all schemes for the prevention of Schistosomiasis are:
- A. Destruction of the adult parasite.
 - B. Prevention of the miracidia from reaching the water.
 - C. Eradication of the intermediate hosts.
 - D. Prevention of cercaria from reaching its hosts.
- (2) A. The establishment of treatment camps was the method adopted in S. Africa in this direction. Mobile hospitals as used in Egypt are not practicable in S. Africa.
- (3) Christopherson's doctrine for eradicating the disease is "no infected humans, therefore no infected snails."
- (4) B. The mentality of the "poor white" and the ignorance of the natives are factors favouring the spread of the infection.

- (5) The installation of pit latrines in Japan and placing of certain rivers and streams out of bounds for school children in Sierra Leone has been attempted but the only effective method is educational propoganda.
- (6) C. Eradication of the snail hosts is the only effective method of preventing dissemination of the disease.
- (7) The keeping of Domestic ducks and the stocking of streams with predatory fish has been advised in S. Africa but no scientific investigation as to their value in destroying the snails has been attempted.
- (8) Cawston suggested the poisoning of the snails with the crushed roots of Tephrosia, (the common wild pea) but no attempt seems to have been made in this direction.
- (9) Copper sulphate is of value for killing the snails and in the Transvaal is best used in the Winter time, the non-raining season when the collections of water are at their lowest levels.
- (10) The role the Nile plays in Egypt in the dissemination of the disease has its analogy in the irrigation schemes in S. Africa.
- (11) The government construction of a dam at Hartbeespoort without utilising methods for controlling the molluscan hosts is a matter of regret. Since construction of this dam the

prevalence of bilharzia in the country supplied with its water is increasing.

- (12) D. The custom among certain tribes of natives of anointing their bodies with grease may be of prophylactic value in preventing infection with cercariae.
- (13) Storage of water for 48 hours kills the cercariae.
- (14) Fresh-water surface-feeding fish may be useful in destroying cercariae.
- (15) Vegetables should be washed before being eaten.
- (16) Swimming baths should be carefully supervised.
- (17) The Transvaal Bilharzia Committee is doing valuable work by propoganda and educational methods.
- (18) A better appreciation of the position by the medical practitioners is essential.
- (19) South Africa has far too long been guided by Paul Kruger's principle. "Alles zal reg kom" (everything will come right) but there are now hopeful signs of an active interest in the matter.
- (20) A list of recommendations is appended.

APPENDIXTHE RECENTLY INTRODUCED COMPLEX ORGANIC ANTIMONY

- (1) In the attempts at obtaining a compound less toxic and less inconvenient in its administration than antimony tartrate, the example of arsenic was followed.
 - (2) "Stibenyl"; "stibosan" or "471"; "neostibosan" or "693B"; "Sb 212" - Bayer; Antimony Sodium Thioglycollate; Antimony Thioglycollamide; and "Antimosan" or "Heyden 661" were compounds tried and which lead up to the introduction of "Fouadin".
 - (3) In Egypt the use of Fouadin has given results which have greatly impressed the workers there. A full review of the methods employed by them and a comparison of the results obtained from the treatment with Fouadin and tartar emetic, is given. The advantages and disadvantages of Fouadin are summed up.
 - (4) Other workers using Fouadin report favourably.
 - (5) In South Africa the opinion given tentatively after a brief trial is, that "it is a valuable addition to our armamentarium, possessing special advantages."
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