purely physical manner, is an open question. (Leeb, Wells, Lewis). Boudreau believes that iodine is a specific agent in the treatment of tuberculosis and reports favorable results.

In our work on the antiferments contained in tubercle bacilli and in tuberculous caseous material, we found that the enzyme-inhibiting action was due to the unsaturated fatty acid radicals of the lipoids. At first we believed that this action was due entirely to the soaps of the unsaturated fatty acids, but subsequent work showed that a large portion of the enzyme-inhibiting agents could be removed by extracting with chloroform. The substances contained in the chloroform extracts are not active as anti-enzymes when suspended in salt solution, as they are insoluble; but the sodium soaps prepared from these acids are active, and we found that their activity was in proportion to the degree of their unsaturation, but that this action was lost if the acids were first saturated with iodine. These experiments were repeated with the chloroform extracts of tuberculous caseous material and with unextracted caseous material, with the result that the soaps prepared from the chloroform extracts became inactive, and the caseous matter which, previous to treatment with iodine, had not been acted on by trypsin, was now readily attacked. The loss of anti-enzyme action cannot be attributed to any activating influence on trypsin, as iodine inhibits the action of this ferment.

Thus we have definite evidence of the action of the iodids on tuberculous tissue, and the explanation of the well known clinical observation that iodids cause tubercle bacilli to appear in the sputum of patients with pulmonary tuberculosis, though they were previously absent. When iodids are taken into the tissues a portion of the iodine is liberated and combines with the unsaturated carbon atoms of the fatty acids. As soon as this occurs in necrotic tissue to a degree sufficient to lower or remove the antiferment action, autolysis ensues, as in most instances ferments are present. That the inorganic iodids diffuse readily throughout caseous matter and are thus in a position to furnish the iodine, has been shown by Loeb and Michaud, and Wells and Hedenberg.

SYPHILIS

Clinical experience teaches us that in the tertiary stage of syphilis iodine is almost a specific in bringing about the amelioration of symptoms, and the disappearance of lesions, and yet little is known concerning the means by which these results are obtained.

Authorities on this subject are unanimous in the belief that iodids are not curative in the sense that they prevent the return of the lesions; this can be accomplished only when the iodids are combined with some other form of treatment. Tomaszewski found that the administration of iodine does not prevent the development of experimental syphilis in monkeys and rabbits; neither has it a curative action; but iodized animals recovered quickly when given mercury. That iodine does penetrate into syphilitic tissues has been shown by O. Loeb.

As experimental work and clinical observations have demonstrated that the iodids do not destroy the infecting organism, we must assume that the results obtained are due to the power the iodids possess of causing resolution of the lesions present. That this actually occurs will be attested to by every clinician of experience.

Owing to its scarcity we have not been able to examine material from gummata, and so we are unable to state positively that the anti-enzymes present are similar to those found in tuberculous caseous matter, but it is probable that the same agents are active here as in those anemic infarcts in which autolysis does not occur. If this assumption is correct, it is not difficult to explain why large gummata rapidly disappear when the patient is brought under the influence of iodids. It is due to the fact that the unsaturated fatty acid radicals which inhibit autolysis, have become saturated with iodine. As soon as this occurs, the ferments which are present, or which may be brought in, become active, autolysis takes place, and the necrotic tissue is absorbed. Here, also, the local action of the ferments is made less difficult by the reduction of the anti-enzyme in the circulating blood. It must be borne in mind that the iodids are not as effective in the earlier stages of syphilis when necrosis of tissue is not so evident.

If the above interpretation of the action of iodine is correct, it gives the clinician a rational idea of what he is accomplishing when he gives iodids to a patient in the tertiary stage of syphilis. According to this view, iodine neutralizes the action of the agents which prevent resolution and absorption of the diseased or necrotic tissue, and at the same time lays bare to the action of the real germicidal agent the infecting organism which previously had been protected by the necrotic tissue. With the exposure of the infecting organism, such agents as mercury and salvarsan would be much more effective.

CONTRIBUTION TO THE STUDY OF THE VALUE OF QUININIZATION IN THE ERADICATION OF MALARIA

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My excuse for adding this paper to the already rather voluminous literature on malaria prevention is that it embodies the result of a unique experience, and one which, I feel, should be recorded.

My principal duty in Daressalam was to institute a campaign against malaria, and although my training has been almost entirely along the lines of attack on the anophelines (in Panama), I was under the impression, formed from the perusal of Claus Schilling's article in Ross' "Prevention of Malaria," that the method of Koch, introduced in Daressalam by Ollwig¹ in 1901-1903, has been successful in so far as it has at least considerably reduced the incidence of malaria.

The results of my study of the conditions in Daressalam have been embodied in a report to the imperial governor of German East Africa, but I was impelled to the writing of this paper by the appearance of Henson's article,² and the wish to show, by citing the results achieved by such an attempt, the difficulties in the way of reducing malaria to any reasonable extent by systematic quinization in a com-

1. Ollwig: Die Bekämpfung der Malaria, Ztschr. f. Hyg. u. Infektionskrankh., 1903, xliii.

2. Henson, Graham E.: Man, the Principal Etiologic Factor in the Perpetuation of Malaria, with Special Reference to the Endemicity of the Disease in the Temperate Zone, THE JOURNAL A. M. A., May 2, 1914, p. 1374.

munity of considerable size. Let me say here that I do not wish to be understood to the effect that the attempt should never be made, that this method of prophylaxis stands condemned as useless. It may have a certain degree of usefulness, but it is, much to my regret, a very insignificant degree when applied to a permanent community of considerable size in a country where anophelines capable of transmitting malaria abound, and where, in addition, changes of population due to immigration serve to introduce more or less continuously gamete carriers.

Daressalam is a town of about 23,000 inhabitants, of whom approximately 1,000 are whites and Goanese, and the remainder mostly Swaheli of Negro-Arabic descent. The town is divided into practically two settlements: the white quarter, situated along the beach, and the native quarter, farther inland. To the east of the town is the Indian Ocean, to the south the harbor and Geresani Creek, a rivulet divided from the harbor by a dam and forming behind it a swamp about $\frac{8}{10}$ of a square mile in area. This swamp and the creek itself are prolific anopheline producers. The distance from the dam to the center of the town is about a mile.

In the very center of the native quarter are two large pools, one permanent, and the other containing water only during the rainy seasons, of which there are two annually. Both of these breed anophelines. One of these, to which reference will be made later, known as Karavanserai Pond, has recently been cleaned out and the banks trimmed, and it is being periodically treated with a phenol preparation. While thus treated it has remained free from mosquito life.

Then there was also, until very recently, a swamp, heavily infested with anophelines, about a mile long and 50 yards wide, in a valley on the very edge of the native town, with a branch toward a small European suburb. This swamp drains into the Msimbasi rivulet, the banks of which are also breeding grounds for anophelines during the dry seasons, and which winds its way in close proximity to the native town.

Across the narrow inlet to the harbor, and less than a mile away from the town, are a number of mosquito-breeding pools and swamps.

The town has no public water supply, nor any sewerage system.

There are about 200 wells, most of these badly covered and containing anopheles larvae. The European houses mostly have pits, into which the sewage is water borne. For this service water tanks are installed under the roofs, few of which are free from mosquito larvae. In addition, anopheles larvae were found in roof gutters.

In the rainy season pools of water, which stand for weeks in many instances, form in numberless places on streets, lots and in yards, and very soon mosquitoes breed in these.

Ollwig arrived in Daressalam apparently firmly believing in the soundness of Koch's theory³ that malaria can be eradicated by attacking the parasite within the human host. He also believed, as he states in his articles in the *Zeitschrift für Hygiene und Infektionskrankheiten* and in private letters to Koch, since published, that a campaign against the mosquito in Daressalam was certain to be fruitless. He lays particular stress on the opinion of an unnamed "expert engineer" that the most prolific anopheles-producing

area, the swamp at the mouth of Geresani Creek, is undrainable. Let me here remark, by the way, that a survey showed this swamp to be drainable, and that when I left Daressalam the creek and swamp were practically free from mosquito larvae, as a result of clearing the creek and ditching, which was done only on a small experimental scale because of the absence of funds.

Ollwig therefore instituted his campaign on the lines of an attack on the parasite in the human host, and this campaign is, so far as my information goes, still continued; at least, it was being continued when I left Daressalam in March of the present year.

The campaign is carried out on the following lines: Blood specimens are taken from all natives employed or living within the European quarter and in the immediately adjacent area. "Thick" smears are made, stained with Giemsa stain and examined. All those whose blood shows the presence of malaria parasites are given 1 gm. of quinin daily for six days and 1 gm. twice a week for ten weeks. The quinin is given in solution and is taken in the presence of a trained nurse.

The accompanying tables show the results accomplished. They have been compiled by Dr. Manteufel of the Daressalam Research Institute. The figures are from carefully kept records, and are not subject to the usual errors of such compilations.

TABLE 1.—MALARIA AND HEMOGLOBINURIC FEVER—MORBIDITY AND MORTALITY AMONG EUROPEANS IN DARESSALAM

Fiscal Year	Population	Morbidity—Percentage of		Mortality—Percentage of	
		Cases	Population	Cases	Population
1903-04.....	377	168	44.5	0	0
1904-05.....	350	141	37.1	3	0.8
1905-06.....	657	355	54.0	4	0.6
1906-07.....	851	287	33.7	6	0.7
1907-08.....	827	268	29.8	6	0.7
1908-09.....	743	342	46.0	3	0.4
1909-10.....	750	506	67.5	5	0.7
1910-11.....	930	460	49.5	10	1.1
1911-12.....	1,024	667	65.2	11	1.1

TABLE 2.—INCIDENCE OF MALARIA INFECTION AMONG THE NATIVE POPULATION OF DARESSALAM BASED ON BLOOD EXAMINATION

Fiscal Year	Adults		Children	
	Examined	Infected Per cent.	Examined	Infected Per cent.
1904-05.....	8,000	10	None examined	
1905-06.....		No examinations made		
1906-07.....	14,752	7.5	3,234	18.9
1907-08.....	15,263	15	4,352	27.0
1908-09.....	28,267	14	3,747	33.4
1909-10.....	17,889	21	5,563	29.4
1910-11.....	15,960	18	4,136	27.7
1911-12.....	24,917	17	4,800	25.1
1912-13.....	19,782	20	3,308	32.0

Manteufel in his paper,⁴ from which the tables are abstracted, says:

When the above-mentioned expedition [Ollwig's] commenced its work in Daressalam, the Europeans were already in the habit of using mosquito bars on beds. However, the use of mosquito gauze for the protection of dwellings, and the taking of quinin prophylactically, as well as measures against mosquito pest, were only gradually introduced during the following years. In considering the influence of Koch's method upon the malarial morbidity of the European population, the above-mentioned factors must naturally be taken into consideration.

Now, the objection may be raised that the quininization was extended to only a portion of the population. The answer to this is that it represents a comparatively steady part of the population: house servants and

3. Koch, R.: Die Bekämpfung der Malaria, Ztschr. f. Hyg. u. Infektionskrankh., 1903, xliii.

4. Manteufel: 12 Jahre Malariabekämpfung, etc., Ztschr. f. Hyg. u. Infektionskrankh., 1913, lxxvi.

artisans, who are less subject to migration than the traders, porters and agricultural laborers, who make up the remainder of the population of Daressalam. It follows that the results obtained among these people would be rather better than the average.

It is recognized, of course, that by leaving the bulk of the population untreated, the chances for infecting the treated portion remain very good.

An experiment was therefore instituted by me to determine the effect of treating all the inmates of a closed community.

For this experiment the negro pupils of the Daressalam Trade School, who live in dormitories and do not come into contact with the outside population, were selected. The school is in the European quarter. Five days after the school was opened, April 6, 1913, blood specimens from all the pupils were examined. One hundred and thirty-one of these were natives of Daressalam; of these sixty-six, or 46.8 per cent., had malaria parasites. One hundred and twelve came from the country; of these fifty-two, or 45.5 per cent., were infected.

All those found to be infected were put on the routine treatment with quinin, and this treatment was continued until Oct. 29, 1914. November 11, the blood of all was examined; 26.4 per cent. were infected with malaria.

The school was closed for the Christmas holidays. Jan. 15, 1914, again five days after the school was opened, 254 pupils were present. Of the 152 who spent the holidays in Daressalam, fifty-one, or 37.4 per cent., were infected with malaria. Of the 102 who spent the vacation in the country, thirty-seven, or 36.2 per cent., were infected with malaria.

A parallel inquiry was carried out. Oct. 3, 1913, 100 adults and fifty children living in the vicinity of the mosquito-breeding pond mentioned before, Karavanseraï Pond, had their blood examined by the same person who examined the blood of the schoolchildren, and who had no idea whatsoever of the purpose or nature of the experiment. None of those examined had ever taken quinin prophylactically, and the subjects were taken at random from the huts in the vicinity. Of the adults thirty-two harbored the parasites of malaria (32 per cent.); of the children twenty-six were infected (52 per cent.).

The pond was cleared of vegetation, the banks trimmed, and the water near the banks treated every ten days with a phenol preparation. The work of clearing was completed in November, 1913. Feb. 26, 1914, again 100 adults and 50 children were taken at random from the population residing in the vicinity of the pond. None of these had had quinin. The blood smears were examined by the person who made the first examination. Of the adults fourteen, or 14 per cent., were infected with malaria; of the children sixteen, or 32 per cent., a decrease of 18 and 20 per cent., respectively.

Among those treated with quinin according to the Koch-Ollwig method, the decrease in a community under ideal control was 13.9 per cent.

It is to be noted that the climatic conditions remained practically constant during the period covered by the inquiry. It is also to be noted that the control of the one breeding area did not by any means eliminate anophelines from the vicinity from which the subjects were drawn. The number of anophelines was reduced, however, to quite a marked extent in such areas.

I want to draw attention to one other factor in connection with the experience in Daressalam with the Koch-Ollwig method.

In the past two years the energetic medical adviser to the governor, Generaloberarzt Dr. Meixner, has had quite a number of measures introduced, all of which tended to decrease the number of anophelines in Daressalam. Unfortunately, conditions are such that Dr. Meixner and his associates are not in a position to carry into effect all the measures against malaria that they rightly consider necessary. The power of the able and zealous officers is greatly curtailed and hampered in East Africa, and their efforts are rendered almost sterile by passive and active resistance, lack of funds and "red tape" in volumes beyond the comprehension, I fear, of the average American.

A COLLOIDAL COMPOUND OF STRYCHNIN AND ITS PHARMACOLOGY *

HUGH McGUIGAN, M.D.

CHICAGO

The migration of drugs in the body, and consequently their action, is largely dependent on their diffusibility through colloidal membranes and their interaction with colloidal bodies. Since I wish to present the action of a colloidal compound of strychnin, it may be of interest at first to give a brief summary of the properties of colloids.¹

In 1861, Graham found that not all substances acted in the same way when their solutions were separated from water by a parchment membrane. Crystalline substances like sodium chlorid, potassium iodid, sugar and the like passed through, while substances like gums, starches and proteins did not. Those that passed through he called crystalloids, those that did not, colloids.

This difference in diffusibility is perhaps the most striking distinction between the two classes of substances; it is not, however, the only one nor is it an absolute one, since all these bodies diffuse to some extent, at least on longer standing.

THE NATURE OF THE COLLOIDAL SOLUTION

Various facts indicate that colloidal solutions are not true solutions but more of the nature of suspensions of fine minute particles of one form of matter in another. The solid particles are separated so that they do not come in contact with each other and are known as the disperse phase. The liquid molecules touch each other and are for this reason called the continuous phase of the colloid. All colloids are made up of these two phases—disperse and continuous. A difference in the size of the particles causes a difference in the refraction of light and consequently a difference in the appearance or color of the solutions. In the crystalline state it is well known that copper sulphate is blue, but if this be finely powdered it is white. Similarly the red oxid of mercury becomes yellow when more finely divided. For the same reason a colloidal solution of gold may be pink, red or purple in water and blue in organic solvents. The ultramicroscope also shows that many colloidal solutions contain fine particles.

* From the Laboratory of Pharmacology, Northwestern University Medical School.

1. This summary is taken mainly from an Introduction to the Chemistry of Plant Products by Haas and Hill, Longmans, Green & Co., London and New York, 1913, p. 273.