from these two organisms were repeatedly given, guided by the opsonic index, and no material improvement occurred, which could not be attributed to local and constitutional treatment coincidentally carried out.

CASE XVIII. Mr. S., fifty-two years. Subacute phlegmon. Two years ago, while in Egypt, had a very acute phlegmon of the cheek, for which he was operated upon in Cairo, and had at the same time very large and often repeated inoculations of antistreptococcic serum. Since then, in various parts of his body, never in any joint, but usually in close proximity to some large articulation, he has had more or less subacute phlegmons. One of these, close to the elbow joint, was incised and a pure culture of the staphylococcus aureus was obtained. From this culture a vaccine was made and the patient was given several inoculations of this vaccine without any appreciable benefit.

The next 2 patients had intermittent hydrops.

CASE XIX. Mr. R., thirty-six years. Intermittent hydrops. Psoriasis. For seven years has had at irregular intervals an intermittent swelling in both knees and both ankles. Associated with this condition has been a very general psoriasis. When, as has happened on several occasions, he has had freedom from joint symptoms for six months at a time, he has also been entirely free from psoriasis. The knees have caused him the greatest inconvenience. The right one has been the more swollen and has had a five-day interval between attacks. The cycle for the ankles was not as clearly defined and he had never taken the trouble to determine it. The capsular swelling in the knees wholly disappeared. The right knee-joint was subjected to an arthrotomy with the hope that the cycle might be broken up. A culture taken from the interior of the joint gave the staphylococcus, which seemed a peculiar bacteriologic finding, but a vaccine was made from the culture and was regularly administered. For three months the operated knee showed no signs of an intermittent swelling. The left knee during this period was less inclined to swell, but did so to some extent. At the end of this interval the right (operated) knee returned to its cyclic distention, though the enlargement has not been as great as before. Observations upon the opsonic index at first showed that it was low to the staphylococcus, but later on the streptococcus seemed to be the organism which showed a low index, and accordingly a streptococcus vaccine was substituted, but without any alteration in progress of the trouble.

CASE XX. Miss S., thirty years. Intermittent hydrops. Both knees have swollen alternately every seven days for over two years. Two days were required for the swelling to attain its maximum and recede. The swelling caused a little pain for a few hours, but chiefly inconvenience from the enlargement. Her serum was tested and found to be low to the streptococcus. A vaccine was injected regularly for some time, but not carefully watched with opsonic tests. The patient has been taking Fowler's solution alternating with quinine during this entire period. There have been two intervals of two weeks each when there was no appreciable swelling in either joint, but this has occurred before under other treatment and no treatment. The amount of swelling is decidedly less, though except for the two intervals cited, there has been no intermission of the regular cycle.

Discouraging as these cases are, looked at from the clinical point of view, it must be remembered that we have been applying a new method, the shortcomings of which are not at present wholly understood. Circumstances have sometimes ex-

isted making it impossible that some of the conditions imposed by laboratory investigators could be carried out. It may be that cases have been treated with vaccines made from organisms having no possible kinship to the organisms originally present in the patient, though the opsonic findings have pointed that way. Again it may be possible that some of the conditions treated were not originally caused by an infective agent. These and many other obstacles stand in the way of drawing conclusions from the results of the first year's clinical experience. A good many more cases were treated and tested than have been recorded here, but those selected for report were chosen because they covered the types of cases most satisfactorily. It would have been possible to select a group, perhaps an equally large one, where the conformity of the opsonic and clinical findings would have been entirely favorable to this new method of study. So in the matter of treatment, typical opsonic charts might have been exhibited corresponding to remarkable degrees of clinical improvement. The writer believes the danger of expecting too much from an untried method is greater than that of expecting too little, and is desirous of encouraging the continuance of trials now going on in the laboratory provided they can be checked by unbiased clinical observation.

DISCUSSION.

DR. L. S. MEDALIA, of Boston: I wish to say that some of the cases that Dr. Painter has mentioned have not been under treatment since the first of February. There are a few cases at the Good Samaritan which have been treated up to date, but those at the Carney Hospital have not been followed up since February 1.

I would emphasize the fact that this treatment has to be carefully and energetically carried out, for the conclusions drawn from those not followed up properly have been unsatisfactory.

THE SERUM TREATMENT OF EXOPHTHALMIC GOITER. A REVIEW OF THE LITERATURE.

BY FRANK S. BULKELEY, M.D., AYER, MASS.

UPON looking over the available literature on exophthalmic goiter, one is at once struck by the fact that drugs having very different actions are, or have been said to be, of benefit. Much of the treatment has been purely symptomatic, perhaps necessarily so. It is hard to see how many of the drugs used could have any influence on the causative factor in the trouble, and their main, if not only, value seems to have been in palliating certain symptoms. This leads us to ascribe the reported cures to general hygiene and the tendency to spontaneous recovery that certain cases show. In a general way such drugs may be divided into four classes: "Nerve sedatives," "vascular sedatives" and cardiac stimulants,

gastro-intestinal antiseptics and laxatives, and general tonics, so-called. Many of the results seem, in the light of more recent investigations, mere coincidence, and the fact that spontaneous recovery occurs at times lends strength to this view. Among the various drugs used, belladonna, ergot, intestinal antiseptics and laxatives of various sorts, strophanthus, digitalis, phosphorus, sodium salicylate, bromides, iron and quinine hydrobromate are, perhaps, the most generally used. Forchheimer speaks very highly of the last named drug, and many reports favorable to its use are on record.

The first signs of an attempt at a specific treatment were seen in the use of milk and blood serum from thyroidectomized animals. This has been followed by an attempt to obtain a specific antitoxin by Rogers and Beebe of New York. They report 90 cases, of which 23 were pronounced cured, 52 improved, 11 were not benefited, and 4 died. The cases were of all grades and at all stages. Some of those reported as benefited may later prove to be cured, and some of those not benefited may show improvement. The originators of the serum state that the chronic toxic cases are the most resistant. The dosage and possible limitations of the serum do not seem to be generally understood, and for further details one should consult the original articles.²⁴ Their serum is a very different thing from the sera prepared by the various manufacturers, and calls for separate consideration. I have had no experience with it, and shall not include it in this review. I have collected the following cases from the available literature:

Enriques.¹ Reports in 1895. Nine cases treated with serum from a thyroidectomized dog. Exophthalmos and all other symptoms relieved. A further report in 1903 says end results are disappointing.

Lanz.² Six cases treated with milk from a thyroidectomized goat. One case treated two weeks. Pulse before, 90; after, 70. Goiter less, and general symptoms much improved. One case treated nine weeks. Pulse before, 134; after, 88. Goiter less and all symptoms benefited. One case treated three months. Pulse before, 150; after, 80. Goiter less. Feels completely cured. One case treated three months. Pulse before, 130; after, 80. All symptoms benefited. Previously bedridden, now able to work. One case treated three months. Pulse before, 130; after, 60. Later went through pregnancy and labor without trouble. One case treated three months with great improvement.

Burghart.³ Three cases treated with the blood of a myxedema patient. Gain in weight and remission of all symptoms.

Moebius.⁴ Two cases treated with Moebius' serum. Marked alleviation of symptoms in both cases.

Schultes.⁵ One case of three years' duration treated with Moebius' serum for six weeks. Pulse before, 240; after, 90. General and mental symptoms much improved.

Goebel.⁶ One case of ten years' duration

treated a few weeks with milk from a thyroidectomized goat. Previously bedridden, now able to walk a mile without fatigue.

Kuhneman.⁷ One case of six weeks' duration treated with rodagen for one month. Pulse before, 140, after, 90. All symptoms gone, gained twelve pounds. Reported later as completely cured.

Murray.⁸ Two cases treated with Murray's serum. Moderately good results in both cases but is not sure it was due to serum.

Thirniger.⁹ Two cases treated with Moebius' serum. Both benefited. One, an acute case of five days' duration, apparently saved from death by two weeks' treatment.

Hempel.¹⁰ One case of six weeks' duration treated with Moebius' serum for one month. Pulse before, 180; after, 90. Total of 90 G. serum used. Patient satisfied with her condition four months after treatment was stopped.

Moussu.¹¹ One case treated with parathyroids of a cow. Gained, but died later of tuberculosis.

Macullum.¹² One case treated with parathyroids of a cow with no result.

Christian. Eighteen cases treated with thyroidectin. All considerably benefited.

Kuh.¹⁴ Ten cases treated with thyroidectin, and one with Moebius' serum. "An excellent palliative but am not certain of permanency of results." All symptoms rapidly improved. In one severe case patient has had no symptoms for two and a half years.

Mix.¹⁴ Two cases treated for a long time with small doses, Moebius' serum. Both are at work with a complete disappearance of all symptoms.

Vanderhoof.¹⁵ Two cases treated two months with thyroidectin. One able to work as hard as ever without trouble. One much improved, but not able to work at time of report.

Waterman.¹⁶ Five cases treated with Moebius' serum. Two cured, free from all symptoms for six and eighteen months. Two benefited, and one not improved.

Rydel.¹⁷ Four cases treated with rodagen with benefit, but is not sure it is due to serum.

Siegel and Ewald.¹⁸ Four cases treated with rodagen with no result.

Adams.¹⁹ One case of three years' duration treated with Moebius' serum for one month. Previously bedridden, but has been at work six months without symptoms.

Kirnberger.²⁰ Two cases treated with rodagen with disappearance of all symptoms and general improvement.

Peters.²¹ One case treated with Moebius' serum with good results.

E. Von Leyden.²² Three cases treated with Moebius' serum. One case of three years' duration. Pulse before, 96; after, 80. Marked general improvement. One case of two years' duration feels much better. One case cured by eighteen months' treatment.

Sainton. Three cases treated with blood of a thyroidectomized sheep. One case treated eight months. Pulse before, 115; after, 80. "Patient transformed into new and healthy woman."

Number of cases.	Reported by	Duration of disease.	Length of treatment.	Serum used.	Pulse before.	Pulse after.	General symptoms.	Benefited	Not Benefited	Goiter	Remarks.
3	Thirniger, 1905			Moebius'			Benefited	3			One, an acute case of five days' duration, apparently saved from death.
1	Hempel, 1905	6 weeks	4 weeks	Moebius'	180	96	Benefited	1		Less	Patient satisfied with her condition four months after treatment.
18	Christian, 1905			Thyroidectin			Benefited	18			
11	Kuh, 1905			10 Thyroidectin, 1 Moebius'			Benefited	11			No symptoms two and a half years after treatment in 1 case.
4	Rydel, 1905			Rodagen			Benefited	4			Not sure it is due to serum.
2	Mix, 1905		A long time	Moebius'			Benefited	2			Possible cures.
4	Siegel and Ewald, 1905		3 months	Rodagen				4			
1	Adams, 1903	3 years	1 month	Moebius'			Benefited	1			
9	Enriques, 1895 and 1903			Serum of thyroidectomized dog			Benefited	9			End results in 1903 said to be disappointing.
6	Lanz, 1899 and 1903	3 months	2 weeks 9 weeks 3 months 3 months 3 months 1 year	Serum of thyroidectomized goat	90 134 130 150 130 ?	70 88 80 80 60 ?	Benefited			Less Less Less Less ? ?	Five possible cures.
3	Burghart, 1899			Blood of myxedema patient			Benefited	3			Gain in weight in all cases.
2	Moebius, 1901	4 years 2 years	52 days 3 months	Moebius'	134 120	110 90	Benefited	2			
1	Schultes, 1902	3 years	6 weeks	Moebius'	240	90	Benefited	1			
1	Goebel, 1902	10 years	A few weeks	Thyroidectomized goat's milk			Benefited	1		Less	
1	Kuhneman, 1904	6 weeks	4 weeks	Rodagen	140	90	Benefited	1		Less	Reported later as completely cured.

2	Murray, 1904	18 months 5 years	2 months 3 weeks	Murray's		Benefited	2	Not sure it is due to serum.
2	Kimberger, 1903			Rodagen		Benefited	2	
1	Peters, 1905			Moebius'		Benefited	1	
3	E. Von Leyden, 1904	3 years 2 years 1½ years	1½ years	Moebius'	96	Benefited Benefited Benefited	80	One reported cured by eighteen months' treatment.
3	Sainton, 1904	8 months 6 months 3 weeks		Moebius'	115 120 134	Benefited Benefited Benefited	80 100 84	One case reported "cured, but has to continue serum."
2	Vanderhoof, 1906	3 years	2 months 2 months	Thyroidectin	140 120	Benefited Benefited	95 ?	One at work without symptoms.
5	Waterman, 1906			Moebius'		Benefited	4	Two cured, two benefited, one not benefited.
1	Bulkeley, 1907	About 8 months	About 4 months with serum	Moebius' thyroidec- tin	100 to 140	Apparently aggravated	1	Patient greatly improved, but quite certain it is not due to sera, as they seemed to aggravate symptoms.
86	Totals,						80 6	Sixteen possible cures judging from data given.
PARATHYROIDES.								
1	Moussu, 1904						1	Gained, but died later of tuberculosis.
1	Macallum, 1905						1	
4	Walsh, 1905						2 2	One severe case not benefited, 2 mild cases apparently benefited, 1 severe case aggravated. Not certain there was no thyroid admixture.

One case treated six months. Pulse before, 120; after, 100. Great improvement, but has to continue serum. One case of three years' duration treated three weeks. Pulse before, 134; after, 84. "Cured but has to continue serum."

Walsh.²³ Four cases treated with parathyroids of a cow. In two mild cases seemed to have a good effect. One severe case not benefited, and symptoms aggravated in one case. Not certain that substance used was free from thyroid admixture.

Billings.²⁹ Reports 12 cases treated with thyroidectin with varying results, but in no case did he secure the favorable results recorded elsewhere. In 1 case Moebius' serum and quinine hydrobromate were used, with resulting steady and continuous improvement.

In the majority of the cases reported not enough detail is given to allow one to judge of the probability of cure, or of the permanency of results. One case reported by Lanz was able to go through pregnancy and labor without trouble. In view of the tendency to increased thyroid secretion in pregnancy, this may, perhaps, be called a cure, although we must admit that such a tendency is not constant. Lanz reports 3 other cases that seem possible cures. Schultes, Goebel and Kuhnenan report cases that might be considered permanently cured. One of Hempel's patients was satisfied with her condition four months after treatment was stopped. Kuh reports that one patient is free from symptoms two and a half years after stopping treatment. Mix, 2 possible cures. Waterman, 2 cures of six and eighteen months' duration. Sainton, 1 case cured. Von Leyden, a case cured by eighteen months' treatment, etc. Nearly all the writers quoted report improvement, and we may, perhaps, be warranted in accepting the statement made by Elsner and Wiseman²⁶ that the palliative action of the serum seems certain and a cure may be possible. They say, "Improvement usually begins within seven days, and that if there is no improvement in three or four weeks the chances are against ultimate benefit. Tachycardia, tremor and precordial distress show the greatest improvement. Cases without marked goiter, with slight tremor and exophthalmos yield most readily. There usually is an increase in weight. Continued use of the serum may be necessary." My experience with the serum is too limited to allow me to venture a decided statement, but I cannot agree that the palliative action of the serum is certain, however probable it may seem. Osborne²⁶ states that there is no doubt that the proper treatment of exophthalmic goiter is by antithyroid preparations, but he is not certain whether the treatment can be pushed or prolonged with safety. The assertion has been made that the sera occupy the same relation to exophthalmic goiter that thyroid extract does to myxedema, but such a statement can hardly be accepted on the evidence at hand. It seems as if the writers used the term cured in a very different way. Some do not report cure where it seems probable; others claim it where only pallia-

tion of symptoms seems certain. It is desirable that a cure in this condition be more exactly defined.

A contrast of the different sera offers little of value. Two observers report 4 cases in which rodagen was useless, although other reports are favorable to it. The other sera seem to have given uniformly good palliative effects. Practically all the writers quoted report improvement, far too many to have it seem coincidence. It seems as if the treatment is at least worthy of a trial in every case. An estimate of the cures from the data given is very difficult, and I shall attempt no such estimate.

I have made use of the sera in one case with very doubtful results. In this case, goiter was slight or absent, tachycardia and tremor well marked, exophthalmos absent, and the other symptoms those usual in such cases. The thyroid was palpable and visible, but at the same time was no larger than is common in many healthy women. Thyroidectin was used in increasing doses. For a time it seemed to be of some benefit but this effect was soon lost, in fact it seemed to aggravate the symptoms. Later, Moebius' serum was tried with practically the same results. Quinine hydrobromate was used for about five months, in doses just under that necessary to produce cinchonism. It seemed to give positive results. Although the amount of bromine in this preparation is small, a daily dosage of 16 gr. was sufficient to cause a well marked bromic acne in this case. Because of the small amount of bromine in the drug it did not seem probable that the bromide action could be the main factor giving relief. For this reason quinine valerianate was substituted, and while it was used for only a short time, the results obtained seemed to equal those from the hydrobromate. The bromic acne produced soon disappeared after the drug was stopped. At present, while it is too early to make a positive statement of results, the patient has gained in weight, has made little or no complaint of tachycardia for six months, and has little or no tremor. Her main complaint is occasional undue fatigue from very ordinary causes, which seems to be growing less marked. Some flatulency, and a tendency to insomnia and anorexia are about the only other symptoms left, and she has been subjected to the two latter ones for years. She is able to go about a great deal with no trouble, and does all her household work. Pulse records taken at random during the past six months have been from 70 to 85, although it is possible that higher records could have been obtained. During the height of the trouble a record of 100 was the rule, and 120 to 140 was no exception. She has had no medicine for about six months. Rogers and Beebe state that some of their cases showed no improvement at the usual period for it to commence, but that it came on after a long interval. It may be that this was the case in the present instance, but the nature of the two remedies and their probable mode of action are so different that it seems improbable. It also seems im-

possible to say that any delayed improvement was not due to a tendency to spontaneous recovery, or to some other means of treatment. I certainly can trace no benefit directly to the serum in this case.

In arranging the cases in tabular form I have included all cases under the terms "benefited," or "not benefited." The probability, or otherwise, of cure, I leave to the individual reader to determine. Thirteen cases reported by Billings are not included in the summary as the details given are very scanty, and no distinct statement of failure to benefit, or of improvement is made.

The tabulated cases appear on pages 28 and 29.

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SYPHILIS AND GONORRHEA IN INTERNAL MEDICINE.*

BY ROBERT N. WILLSON, M.D., PHILADELPHIA.

OF all the economic problems with which this and other nations must deal, none exceeds in difficulty that of venereal disease. Syphilis and gonorrhea have been reaching out for the vitals of more than one race, and have laid hands heavily on the civilized world. Venereal disease forms a serious social, as well as medical, dilemma. To the necessity of applying itself to this dilemma, the public is just opening its eyes.

One needs to look back only a few years to recall a period in which venereal disease was treated as a matter of course, and often as a half joke, by the general practitioner, and if not by him by the druggist, and at a still earlier time, by the barber-at-large. The profession has grown up, as it were, with venereal disease in its midst, unwillingly conscious of the presence of an unwelcome companion, and yet finding its acquaintance more and more intimately thrust upon it as time has flown. The doctor has known syphilis and gonorrhea as the dog knows his enemy the flea, but no more intelligently. Along with the rest of humanity he classed these diseases as necessary evils to be borne with stoicism and to be disregarded when possible, because too closely bound up with the recognized pleasure of

life to admit of a change. The youngest of us can remember the advice of our medical seniors to enjoy our wild oats, because only in such a way could the experience necessary to a doctor be gained. No word was uttered regarding injuries that might accrue to the individual and his home.

Within a few years the medical profession has been learning that syphilis and gonorrhea are factors to be seriously reckoned with. The possibility of the influence of syphilis is considered in every diagnosis, and in the planning of every treatment. Its earmarks stand out upon the highborn and the lowly, the king and his subject, from the grandfather to the third generation. The doctor is to-day hurrying to stem a tide which years ago might have been turned with a finger. He pays no small price for this privilege of serving the people, as is seen in the record of professional accidents that annually result in the syphilization of not a few members of his calling. If there were no other incentive, the danger to which he is daily exposed would commit him to a position in the front line of the battle, now to be waged against a common enemy. The doctor is trusted by the public to a degree that is shared by no other public servant. The laity must simply remind him and keep him faithful to this trust by its interest and encouragement. In one form or another syphilis or gonorrhea enters at some time nearly every home. Their ultimate consequences account for a morbidity and mortality that will exceed that of any given class of disease. The plain physician, the general practitioner, alone knows the full sorrow of venereal infection in the home. He has not realized that the public has for some time been ready for the facts which he has kept in his bosom. Medical literature is full of the material that will rouse the public to action. The people stand at the doctor's door, with hand at ear. What will conservatism and professional ethics allow him to say?

A hurried glance at the literature of syphilis and gonorrhea published during the period 1903 to 1906 inclusive yields the following interesting facts. Four hundred and seventy-five articles have appeared in the leading medical journals, dealing with syphilis alone. The average number of cases of syphilis reported in this series was ten per article; but many included the reports of from 500 to 1,000, and few recorded less than 5. As each instance of syphilitic infection represented at least one other as its cause, this library deals with not less than 5,000 public reports of cases of syphilis, and more much likely 50,000, if the full count were made. During the same period 176 articles appeared upon gonorrhea, a disease which has been discussed, until there is little to say beyond the fact that the profession realizes with each new year how little real knowledge it has upon the subject. The danger is the only settled and established factor, other than the causal germ. Syphilis is at most times a purely medical condition. Only when the internal organs are seriously involved does the syphilitic come for a moment under the surgeon's care. Gonorrhea, on the other hand, has been considered

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