1. What is the Schick test, and what is its importance in the prevention of diphtheria?

2. Discuss the aetiology of undulant fever in man.

3. What evidence is there that scarlet fever is caused by a haemolytic streptococcus?

4. What bacteriological methods are available for estimating the degree of excretal pollution of water?

5. Discuss the rôle played by the bovine tubercle bacillus in the causation of tuberculosis in man.

6. Give a brief description of the typhoid-paratyphoid group of bacilli, including the more important differential characters. Note briefly, in the case of each organism which you mention, the host in which it is commonly found, and the type of disease to which it gives rise in man.

7. Discuss the aetiology of influenza.

8. Describe briefly a method of performing the Wassermann reaction. Discuss the employment of this test in diagnosis and in the control of treatment.

9. Give a brief description of the diphtheria bacillus. What tests would you carry out to establish with certainty the identity of a bacillus isolated from the throat of a chronic carrier?

10. Give a brief description of the meningococcus. How would you distinguish it from the other gram-negative cocci which may occur in the human nasopharynx?

11. Discuss the use of the agglutination reaction in the diagnosis of enteric fever.

12. What is meant by the term "filtrable virus"? State what you know with regard to the virus of vaccinia.

13. Discuss the aetiology of the common cold. Give your views with regard to the protective value of "anti-catarrhal" vaccines.

14. Discuss the bacteriology of puerperal sepsis.

15. Give a brief description of the gonococcus, and discuss the laboratory methods available for the diagnosis of acute and chronic gonococcal infection.

16. Give a list of the various bacteria that may be associated with food poisoning in man. State in the case of each organism you mention (a) the type of illness to which it gives rise, (b) its normal habitat, (c) the type of food in which infection is most commonly conveyed to man, and (d) the method by which the food most commonly becomes infected.
17. You are asked to carry out such bacteriological examinations as you think desirable on a female patient, 29 years of age, who has been suffering during the past 8 days from an irregular pyrexia, fluctuating between 99.5°F and 102.5°F. Apart from the fever, the clinical signs are slight and indefinite. State what examinations you would carry out, and describe in detail the methods you would employ in collecting the requisite specimens for examination. Give a brief description, without technical details, of the way in which you would deal with the specimens in the laboratory.

18. You have received the following report on a sample of water drawn from a household tap connected with the main water supply, in a town which takes its water from an upland surface and purifies it by filtration.

- Number of bacteria growing on gelatine at 22°C in 3 days = 850 per c.c.
- Number of bacteria growing on agar at 37°C in 2 days = 78 per c.c.
- B. coli: present in 10 c.c., absent in 1 c.c.

What conclusions would you draw from this report?

19. You are asked, as a bacteriologist, to investigate an outbreak of tonsillitis which appears to be associated with a particular milk-supply. Describe the examinations which you would make, and discuss the significance of your possible findings.

20. Discuss the aetiology of infective diarrhoea in infants.

21. Describe the more important characters of the pneumococcus, and discuss the value of antipneumococcal serum in the treatment of lobar pneumonia.

22. What is diphtheria antitoxin? How is it standardized? What immunological principles govern its use in (a) the treatment, and (b) the prevention, of diphtheria?

23. How would you examine the carcase of a rat, suspected to have died of plague?

24. Describe and discuss the bacteriological methods available for the diagnosis of tuberculosis in man.

25. Discuss, from the standpoint of the bacteriologist, the measures that you would advise to control an outbreak of diphtheria in a boarding school for boys.

26. Discuss the importance of the human carrier in the spread of enteric infection. What steps would you take in searching for a possible carrier, if you were asked to investigate an outbreak of enteric fever in a large institution?

27. Give a brief description of the forms in which anthrax occurs in man, and the ways in which the infection may be contracted. What bacteriological examinations would you carry out in a suspected case?
28. Describe briefly and compare the various types of _B. dysenteriae_. To what extent and under what conditions do these types cause infection in this country? How could a laboratory diagnosis be made?

29. How would you examine a specimen of cerebro-spinal fluid, withdrawn from a suspected case of meningitis?

30. State what you know of the virus of poliomyelitis. How is the disease transmitted and what specific therapy is available?

31. Give examples of the use of active and passive immunization in prophylaxis against virus diseases, stating briefly in each case the immunological principles upon which the method depends.

32. Give a brief description of the _Streptococcus haemolyticus_ and describe briefly the infections to which it gives rise in man, stating in each case the ways in which infection is usually carried, the lesions produced and the prophylactic or curative measures you would adopt.

33. Discuss the value of bacteriological methods in the grading of milk.

34. What laboratory methods are available for the diagnosis of chronic gonococcal infection? Discuss the relative value of these methods in cases of different type.

35. Give three instances in which a blood culture is of service in arriving at a bacteriological diagnosis. Describe briefly the technique that you would employ in obtaining the specimen, and state in each case the exact method of cultivation you would employ, and how you would identify the organism isolated.

36. How would you examine a sample of potted meat suspected to have been the cause of an outbreak of botulism?

37. Discuss the diagnostic value of tuberculin.

38. What is diphtheria antitoxin? How is it standardized? What principles govern its use in prophylaxis and treatment?

39. Discuss the aetiology of influenza and the common cold.

40. What bacteriological investigations would you undertake before ascribing an outbreak of enteric fever to pollution of a water supply?

41. Describe briefly the Wassermann reaction, with special reference to the principles involved in the test.

42. Describe the process of the pasteurization of milk, and discuss its hygienic advantages and disadvantages.

43. Describe in detail how you would make a bacteriological diagnosis of gonorrhoea in the male.

44. Describe the diphtheria bacillus and explain how it may be distinguished from other bacilli with which it may be confused.
45. What bacteriological and immunological procedures would you adopt to prevent the spread of scarlet fever in a small boarding school?

46. Discuss the aetiology of bacterial food poisoning.

47. Describe carefully what is meant by Active Immunity and compare it with Passive Immunity.

48. Write a short account of the anthrax bacillus and discuss the problem of sterilizing materials contaminated with the organism.
EXOPHTHALMIC goiter, according to the "two-product hypothesis" of H. S. Plummer, is theoretically defined as a constitutional disease dependent on an unknown stimulus on the thyroid gland. It is associated with the production and delivery to the tissues of an abnormal thyroid secretion, and, in practically all instances, of an excessive quantity of normal thyroxin. The nature of the abnormal thyroid secretion is unknown. The progress of the disease is usually by exacerbations and remissions, and there is a tendency for the disease to cease spontaneously after running a course of from a few months to twenty years or more. Previous to the demonstration by H. S. Plummer of the value of Lugol's solution (compound solution of iodine, U. S. P.) in the treatment of exophthalmic goiter, the preoperative preparation of patients suffering from this disease consisted chiefly of two factors: rest, in an attempt, usually ineffectual, to husband the patient's strength, and a program of waiting until a natural remission should allow the patient to show improvement.

The two-product hypothesis offers an excellent basis on which to explain certain characteristics of the disease that are of greatest importance in explaining the results of what has already been proved to be the most efficient form of treatment. The phenomena of the disease which are dependent on abnormal thyroid secretion are the psychic status peculiar to exophthalmic goiter, the useless purposeful movements, stare, exophthalmos, and the gastro-intestinal crisis, with vomiting and diarrhea. These symptoms are associated with a more severe reaction than the symptoms referable to pure hyperthyroidism, and the patient who shows a predominance of the symptoms referable to the abnormal thyroid agent is always potentially in a condition that may be suddenly precipitated into an exophthalmic goiter crisis, the most serious status of the disease. During an exacerbation of exophthalmic goiter, these phenomena are more exaggerated than during a remission. The factor of true hyperthyroidism, that is, the part of the disease due to the production of an excessive normal thyroid secretion, is of much less importance in determining whether a patient is ready for thyroidectomy than the evidence in that patient of intoxication from the abnormal agent. These statements will explain why a patient with a high basal metabolic rate will often be in better clinical condition, and will be a lesser risk for thyroidectomy, than one with a low basal metabolic rate, if the clinical status is associated with a predominance of intoxication in the first case from excessive normal thyroxin, and in the second case from the abnormal thyroid secretion.

Since the value of the administration of Lugol's solution has become established, preoperative treatment of exophthalmic goiter has been revolutionized. The mortality in the medical treatment of the disease has been almost abolished. The time necessary for preparation for operation has been greatly reduced. The surgical mortality has been greatly reduced; according to data recently compiled by Pemberton, the surgical mortality in exophthalmic goiter for the year 1927 at The Mayo Clinic was 0.72 per cent. The necessity for preliminary surgical procedures, such as hot water injections and ligations, has been almost eliminated. Again quoting from Pemberton's data, in 1921, before the use of Lugol's solution was begun, the total number of ligations for exophthalmic goiter was 123 per cent of the total number of cases, in many cases two or more ligations being done; in 1926 and 1927, the number of ligations for each year was 0.6 per cent of the number of cases of exophthalmic goiter. The reactions to Lugol's solution have also offered invaluable information furthering the knowledge of exophthalmic goiter.

Following the administration of iodine in sufficient doses to patients suffering from exophthalmic goiter, certain changes are brought about with predictable frequency: Progress of exophthalmos is stopped, the stare disappears, and the characteristic psychic status and movements are abolished. If the patient is in crisis, the vomiting will be controlled within from twenty-four
to forty-eight hours. The clinical improvement
depends to some extent on the relative amount
of abnormal secretion present in the individual
case; that is, if the patient is manifesting the
foregoing phenomena in association with abnor-
mal secretion, great clinical improvement would
be expected. If, however, the patient showed
marked evidence of hyperthyroidism and fewer
of the phenomena associated with an abnormal
product, the improvement from iodine would be
less. The latter are frequently classified with
those who have suffered from the disease for a
long time and in whom the gland is large and
the basal metabolic rate high. In such case,
the gland has probably been trained by long con-
tinued overstimulation to produce a relatively
high proportion of normal thyroxin. The basal
metabolic rate is usually high, and the drop in
the rate following the administration of iodine
is relatively small. Patients who are admitted
for examination in crisis may or may not have
extremely high metabolic rates; they usually
show, in any event, a proportionately great drop
after the administration of iodine. From clin-
cial evidence, one may predict with considerable
accuracy whether a small or great drop in basal
metabolic rate will result from iodine treatment.

Inasmuch as the administration of iodine con-
trols only one phase of the disease, exophthalmic
goiter, it is necessary to complete the control.
Thyroidectomy seems to be the method pre-
ferred from all points of view, mortality, mor-
bidity, efficiency, and consumption of time in
bringing about control. As has been said, the
natural course of exophthalmic goiter is in waves.
The administration of iodine does not change
that course, but it does control one of the fac-
tors concerned. Thus if its administration is
continued long enough and an exacerbation of
the disease is imminent, the basal metabolic rate
will rise after its initial drop. It is not justifiable
to interpret this rise as due to the action of
iodine. In fact, if iodine is continued the basal
metabolism will drop and the intensity of the hy-
perthyroidism will subside when the natural
course of the disease has progressed to this state.
Patients are not infrequently observed who have
been taking iodine constantly for several months
or a year. They give a history of the usual ex-
cacerbations and remissions, but none of crisis if
sufficient amounts of iodine have been taken.
The patients are, as a rule, in better general
health than would be expected considering the
duration of the disease. Another group of pa-
tients not infrequently seen consists of those
who have taken sufficient amounts of iodine for
a long time, and then stopped it. Usually within
a few days afterward symptoms associated with
the abnormal thyroid agent appeared. Many
patients grew worse rapidly, some of them reach-
ing the gastro-intestinal crisis after two or three
weeks. Patients who have taken iodine con-
tinuously have kept the abnormal thyroid secre-
tion of exophthalmic goiter under control, and
are surely in much better condition than if they
had not taken iodine, or had taken it intermit-
tently; they also avoided the risk of being pre-
cipitated into a crisis. Patients who have gone
into crisis after stopping the iodine may control
it by resumption of iodine. The crisis could have
been prevented by the continuation of iodine.
The observation has been made repeatedly that
cessation of iodine in a case of exophthalmic
goiter will be followed, usually within from four
to six days, by the reappearance of stare, char-
acteristic movements, and psychic status, and a
rise in the basal metabolic rate. This charac-
teristic reaction and its counterpart, the control
of such symptoms by iodine, are of great aid
as diagnostic criteria in certain cases.

In the routine care of exophthalmic goiter, 30
minims of Lugol's solution daily is enough to
control the symptoms attributed to abnormal se-
cretion. Patients in crisis should receive larger
doses, 50 to 100 minims daily, until the crisis
status is under control. If Lugol's solution can-
not be retained when taken by mouth, which is
very unusual, it may be diluted freely with physi-
ologic sodium chloride solution and given by
rectum. It has been given satisfactorily by
stomach tube to unconscious patients. If the pa-
tient is in crisis it is most important that Lugol's
solution should be given in large doses, and re-
tained. Following the foregoing regimen most
patients will be ready for thyroidectomy within
from eight to ten days; those who are first ob-
served in crisis are held for a longer time, how-
ever. Cardiac decompensation, recent infections,
and so forth, necessitate delaying operation for
considerably longer periods. In such cases it is,
of course, advisable to continue the administra-
tion of iodine without interruption.

Cardiac decompensation in cases of exophthal-
mic goiter is usually present only if there has
been preexisting cardiac injury. Auricular fibrillation is a common accompaniment, occurring in 22 per cent of cases. The effect of iodine is frequently striking. The slowing of the pulse, diminution of pulse deficit in cases of auricular fibrillation, and the mobilization of fluids with loss of ascites, hydrothorax and edema, are produced with great rapidity. Only rarely is the use of digitalis necessary or advisable. Since H. S. Plummer has demonstrated the frequent unfavorable effects of digitalis in cases of hyperthyroidism, it has been used in The Mayo Clinic only in rare instances, chiefly in cases in which cardiac decompensation progressed in spite of other therapeutic measures.

Patients suffering from infectious processes, particularly respiratory infections and exophthalmic goiter, are strikingly benefited by iodine. The crisis status apparently reduces resistance against acute infections and the reactions to infection in that state are extreme. Iodine, in controlling the crisis status, permits rapid recovery from the infectious process unless it is too extensive or too far advanced.

Since the institution of iodine, prolonged periods of rest in bed have become unnecessary and inadvisable. Patients lose much strength from the disease, and if this loss is increased by confinement in bed, they may become so weak as to be unable to sit up without help. In extremely severe cases a degree of weakness is reached that makes it impossible for the patients to be out of bed. It is advisable for all patients that are not too weak to be out of bed. In this way much greater general strength is maintained. Patients suffering from cardiac decompensation or acute infections are, of course, kept in bed.

There seems to be no valid reason for restriction of the diet. A diet up to 5,000 calories daily is allowed and no particular article of food is restricted except coffee; thus nutrition is maintained. Most patients on this diet and iodine will soon begin to gain weight.

Iodine in itself should not be considered sufficient for the complete control of exophthalmic goiter. Rarely complete control will be secured in this manner, but in such cases the condition is usually in or near natural remission. If operation is postponed, the patient should be kept under careful surveillance, so that at the first evidence of uncontrolled hyperthyroidism, thyroidectomy may be performed. It is, however, extremely unusual for a case to be so controlled and in the usual case a great injustice is done if further efforts are not made to complete the control of the disease. In the most serious cases, those in which prognosis as regards functional result and surgical mortality is most unfavorable, the disease has existed for a long time. Therefore, it is of great importance that the disease be completely controlled as quickly as possible. Fortunately, patients are now coming for treatment earlier than ever before, and consequently the end-results of treatment will be better. Quoting from Pemberton's statistics, in 1909, the average duration of the disease in patients who came to The Mayo Clinic was thirty-one months. The duration has been steadily decreasing so that in 1927 it was fourteen months. In 1909, only 45 per cent of the patients had had the disease for twelve months or less, whereas in 1927, 77 per cent were in this group. These figures are as reassuring in regard to the morbidity as they are in regard to the surgical mortality. In closing, I wish to emphasize two points:

1. In any case of exophthalmic goiter it is of greatest importance completely to control the disease as quickly as possible; almost invariably this cannot be achieved by iodine alone.

2. The uninterrupted use of iodine should be urged until patients recover from the disease. In any case in which thyroidectomy must be postponed temporarily, the patient should at least be given the advantage of having the most serious phase of the disease kept under control.

BIBLIOGRAPHY

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