stopped. The nausea and vomiting may be a true indication of toxic dosage or merely the outcome of the resentment of an engorged stomach to a nauseous drug. If there is reason to believe that the latter is the case, then the digitalis should be continued, but given well diluted or in a bland bismuth draught. When the tincture is badly tolerated the patient can sometimes take with comfort either Nativelle's digitalin granules or the tincture of strophanthus.

In the mildest cases of all, with only a moderate acceleration of the ventricular rate and no distress, regulation of the life and the exhibition of mild haematinics over a long period yield the best result. There are few better cardiac tonics than an adequate supply of good blood to the heart through the coronaries. This is especially applicable to the cases of fibrillation occurring in patients with high blood pressure and arterio-sclerosis.

Can we Stop Fibrillation?

Sometimes fibrillation ceases spontaneously and may never recur; more often it is permanent. Recently much has been written about the action of quinidine sulphate and its power of terminating fibrillation, and it may be of interest to you to refer to this line of treatment.

My experience covers 17 cases in which I have given quinidine with the object of restoring a normal rhythm. In 6 of the 17 the treatment failed. Either the patient could not tolerate the drug or the cardiac failure was accentuated by the quinidine. In 11 of the 17 a normal rhythm was obtained, but two of these relapsed and persisted in their fibrillation. Ultimately in 9 of the 17 patients the normal rhythm was maintained. (See Fig. 3.) It is possible if not probable that as time goes on some of these 9 may fall from grace. On resumption of the normal rhythm some patients feel materially improved, others do not admit to much, if any, benefit.

In my opinion the treatment is not free from danger, and the action of the quinidine should be most carefully checked. My practice is to have an electrocardiogram taken twice a day and the changes in the auricular and ventricular contractions noted. I give the drug in capsules in doses of 0.2 gram spread over the twenty-four hours, so that the patient receives ten doses, or 2 grams, a day. Its indiscriminate use is dangerous, and it should only be given in carefully chosen cases and with the patient under continuous observation. I should like to emphasize this as I have met several instances where, through ignorance, quinidine sulphate has been prescribed recklessly and without any attempt at adequate supervision.

Summary.

Irregular action of the heart is not merely a matter of degree. The types differ fundamentally and their significance varies widely.

The most important group is that of fibrillation of the auricle, characterized by a specific and fundamental change in the activity of the auricles, and a frequent and disorderly action of the ventricles. This increases the load of the heart and is the most common cause of cardiac failure. The recognition of this form of irregularity is not difficult, requiring only the fingers and a trained intelligence.

Fibrillation is not confined to any one particular form of cardiac lesion, but may occur at any age, and when once established tends to persist.

The digitalis group produces a remarkable slowing of the ventricular rate with consequent improvement in the patient.

Auricular fibrillation can in 50 per cent. of the cases be terminated by quinidine sulphate, but in many patients the fibrillation recurs, and the exhibition of this drug is not without danger.

THE Dutch Society for Combating Alcoholism will hold a Congress at the Hague on September 11th, when the following subjects will be discussed: Alcoholism and criminality, introduced by Professor Bongers, and treatment of chronic alcoholism, by Dr. F. S. Meijers.

ACCORDING to a warning issued by the U.S. Public Health Service, leprosy is on the increase in the United States. Statistics show that there are 1,200 lepers at large in twenty-five States, contact with whom may further spread the disease. It also appears to be prevalent in Latin America, for Dr. R. F. Parra, physician-in-chief of the Agua de Dios Leprosarium, Colombia, reports that there are now 2,726 lepers segregated there. Chaulmoogra oil is being used in the treatment of 122 of these patients.

An Address

ON

ACUTE ARSENICAL POISONING.*

BY

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DURING the last few years our knowledge of the physiological, therapeutical, and toxicological effects of arsenic has been greatly extended, owing largely to the greatly increased use of preparations of arsenic in the treatment of disease. Thus the use of arsenobenzol derivatives for the treatment of syphilis is worldwide, and many other organic arsenical compounds are largely used in pharmacology. In some cases toxicological effects have followed the therapeutic use of these powerful remedies, and a study of these effects has not only enlarged our conceptions of the physiological and toxicological action of arsenic generally, but it has also stimulated the study of the quantitative tests for the efficiency of important organs of the body—for example, the liver.

Application of advances in pathological and chemical technique has enabled the toxicological effects of arsenic to be studied with more precision and detail, and thus has led to an extension of knowledge.

It will be my endeavour to call attention to the recent advances in our knowledge of the toxicology of acute arsenical poisoning, to give a summary of the salient points, and to illustrate them where possible by classical examples. Acute poisoning by white arsenic and similar inorganic compounds will be considered, and reference will be made to poisoning by arsenobenzol derivatives. Arseniuretted hydrogen will not be dealt with.

Arsenic is one of the commonest and oldest known poisons. It is stated to have been discovered in the third century. Its toxicology overshadows that of all other poisons in importance. Its poisonous properties are known to everyone and its preparations are easily accessible. It is almost tasteless, and can be introduced into food without fear of detection. It produces symptoms which closely simulate natural diseases, and it is not therefore surprising that as a homicidal poison it has easily held the first place for centuries.

Arsenical poisoning may be homicidal, suicidal, accidental, or produced when taken for the purpose of causing abortion or as a quack medicine. Out of 1,000 recorded cases from 1752 to 1911 collected by Witthaus the reasons for taking the poison were as follows:

Homicidal...	...	...	...	42.6 per cent.
Suicidal ...	...	...	...	23.0 "
Accidental ...	...	...	...	20.0 "
As an abortifacient ...	...	...	...	3.3 "
Due to quack medicine ...	...	...	...	0.4 "
Motive unknown ...	...	...	...	10.7 "

These figures, however, cannot express the true proportions, since suicidal and accidental cases are commonly not recorded. Homicidal poisoning must represent only a small minority of all acute arsenical cases. It is certain, however, that as a poison used for homicidal purposes the absolute number of cases far exceeds those of any other poison.

Preparations Used.

Arsenious oxide (As_2O_3) is the preparation most commonly used for criminal purposes; it is a white inodorous powder, almost tasteless, and slightly soluble in water; about 1/2 grain dissolves in an ounce of cold water, and 6 to 12 grains in a similar quantity of boiling water. It can be added to food and drink without fear of detection, and persons wishing to use it for criminal purposes appear to have no difficulty in obtaining it.

When sold to the public the regulations of the Poisons Acts should be complied with, and one of the conditions of sale of white arsenic is that it should be coloured by the admixture of at least one-sixteenth of its weight of soot or indigo. The evidence of recent notable trials shows that this rule is sometimes honoured in the breach rather than in the observance (Armstrong case).

An easily available source of white arsenic which is often forgotten is the chemical laboratory. The poison can be

* Given before the Medico-Legal Society, July 4th.

obtained in any quantity from wholesale firms for laboratory purposes without any restriction as regards its sale. Every chemical laboratory possesses large quantities of arsenic easily accessible to anyone visiting or using it.

Arsenious oxide is sold in combination with sodium hydrate or carbonate as weed killer. This may be a strong solution of sodium arsenite containing 14 to 40 per cent. of arsenious oxide. The liquid preparation is usually coloured by the addition of aniline dye such as fluorescein, though during the war it was sold uncoloured. The solid form of weed killer consists of a fine powder usually coloured and containing a high percentage of arsenic. An example of this is Eureka weed killer, which was mentioned in the Greenwood case. A sample was found by Mr. J. Webster to contain 60 per cent. of arsenious acid and to be coloured with phenolphthalein. The powder was very soluble in water and formed a pinkish-red solution which was decolorized by acids.

These preparations are most poisonous; not only may they give rise to accidental poisoning but there is reason to believe that they have been used for criminal purposes on many occasions. An instance of several cases of accidental poisoning due to liquid weed killer occurred in Sussex in 1919, when a sack of sugar absorbed a quantity of liquid weed killer from a leaky tin placed beside it during transit in a railway carriage. The consumption of the contaminated sugar gave rise to acute arsenical poisoning.

In the case *Rex v. Bingham*, 1911, three fatal cases of arsenical poisoning were the subject of inquiry; these were undoubtedly due to weed killer.

In May, 1921, an inquest was held on a woman named Hanktelow at Beckenham, where death was found to be due to acute arsenical poisoning. In this case the source of the arsenic appeared to be Eureka weed killer.

Liquid preparations known as "wood preservatives," similar in composition to weed killer, are used for destroying insects infesting wood. Since these are not coloured there is great risk of accidental poisoning from their use. The liquid may accidentally contaminate food or drink and give rise to acute arsenical poisoning. An instance has recently been brought to my notice where, after treatment of the interior of a large hut with arsenical wood preservative, the dust of the hut was found to contain a considerable percentage of arsenic, and the air of the interior was also contaminated with arsenic. Arsenic in combination with alkali is used largely in the manufacture of sheep dips, and these preparations have sometimes given rise to acute arsenical poisoning.

A solution of lead arsenate is commonly employed in fruit spraying, and cases of severe arsenical poisoning due to these preparations have been under my care.

There is no doubt that the common use of these commercial preparations of arsenic is a frequent cause of fatal arsenical poisoning, and the time appears to have come when the mode of sale of these preparations should be carefully considered with a view to the safeguarding of the public against risk of accidental poisoning and to prevent dangerous homicidal poisons being so easily accessible to persons with criminal intentions.

Other preparations of arsenic such as sodium arsenite, metallic arsenic, arsenic acid and sodium arsenate, copper arsenite (Scheele's green), a mixture of copper arsenite and copper acetate (Schweinfurth green, Paris green, emerald green), arsenious sulphide (orpiment or King's yellow), have given rise to acute poisoning, usually of an accidental or suicidal nature; and the medicinal preparations of arsenic must not be forgotten as causes of acute poisoning when taken in excessive doses.

SYMPTOMS OF ACUTE POISONING BY ARSENIC.

Arsenic is usually described as an irritant poison. It certainly is an irritant, but it does not kill by virtue of its irritant properties on the gastro-intestinal tract. Arsenic is a most powerful tissue poison, and it is to the toxic effect on the important organs of the body, especially the heart, kidneys, and liver, that a fatal result is due.

The importance of the toxic action of arsenic is too often lost sight of in the medico-legal inquiries concerning cases of acute arsenical poisoning, and attention is too much concentrated on the irritant effects of the poison. It is often assumed that the irritant symptoms of vomiting and diarrhoea are the chief cause of death owing to their exhausting effect on the body, whereas it is the toxic action of the poison on the heart and other organs which is usually responsible for the fatal issue. The vomiting and diarrhoea *per se* are rarely of

themselves the cause of death, and indeed these symptoms can be controlled by medicinal treatment.

In his evidence in the Madeline Smith case, in 1857, that great toxicologist Dr. Robert Christison said, on being cross-examined as regards the large quantity of arsenic present in the stomach of the deceased: "The very fact of poison being found in the stomach at all in the case of arsenic shows that more has been administered than is necessary, as it is not what is found in the stomach that causes death but what disappears from the stomach." In other words, Dr. Christison considered that it was the toxic effect of the absorbed arsenic on the important organs of the body which caused death, not the local irritant effect on the stomach and intestines.

The symptoms of acute arsenical poisoning are very variable in their occurrence, and no hard and fast rule can be laid down as to precisely what symptoms will occur and the order of their occurrence. Thus the same toxic dose of arsenic may in one person produce vomiting first and diarrhoea afterwards, but in another person the reverse may obtain. An example of this has recently come to my notice. Then again some symptoms, such as burning in the throat, thirst, or cramp in the legs, may be prominent in some cases but entirely absent in others.

Criminal cases of arsenical poisoning commonly present symptoms which are due to a succession of doses, possibly each sublethal but poisonous. In such cases the symptoms of acute arsenical poisoning, such as would occur from one single dose of arsenic, may be masked by the appearance of symptoms due to the prolonged action of arsenic—that is, to those of subacute or chronic poisoning. Thus symptoms of arsenical neuritis, or of renal or liver disease, may be superimposed upon those of the acute gastro-intestinal symptoms.

When a single poisonous dose of arsenic is taken by the mouth (one or two grains or over) the interval before the appearance of symptoms is variable. Possibly some peculiar taste of a slightly metallic nature may be noticed, but this is frequently absent. Nausea will probably be the first symptom, and this may occur within a few minutes of taking the poison. The onset of symptoms is dependent on the state of the stomach at the time of taking the poison. If empty there will be little if any delay in the appearance of the symptoms. Much depends also on whether the arsenic is in solution or in the solid state; in the latter condition the onset of symptoms will be delayed. Then again, if the arsenic is in the solid form there will be more delay if the solid is insoluble than if it is soluble.

If the stomach contains food the onset of symptoms will be delayed and also if the poison is taken with food, or if food is taken within a few minutes of the poison. Examples of the variable occurrence of gastric symptoms are shown by the recent Armstrong case, where after a possible poisonous dose there was a delay of one and a half hours before the occurrence of nausea, and of three and three-quarter hours before the occurrence of vomiting, and of eight and a half to ten and a half hours before the occurrence of diarrhoea. In this case (Mr. Martin) the poison was no doubt taken in the solid form (arsenious oxide) with tea and scones and bread-and-butter. In a recent very interesting case published by Dr. St. George (BRITISH MEDICAL JOURNAL, February 5th, 1921) a patient at 8 p.m. took about 180 grains of white arsenic in mistake for magnesia; the poison was mixed with hot milk, and half an hour later porridge and milk were taken for supper. It was not until four hours after taking the poison (12 midnight) that vomiting occurred, and this was accompanied by burning pain in the epigastrium and diarrhoea. At 4 a.m. cardiac failure was shown by coldness, feeble thready pulse, and general collapse; cramps in the legs also occurred. Under medicinal treatment the vomiting and diarrhoea were controlled. At 10 a.m. suppression of urine occurred. The patient recovered from the immediate acute symptoms, but a severe multiple neuritis developed, and the patient died from this three and a half months later. This case is a good example of the action of arsenic, which is that of a protoplasmic poison, the irritant effects not being of themselves fatal.

A remarkable example was mentioned by Dr. Christison in his evidence in the Madeline Smith case, in which a girl took a large dose of arsenic at 11 a.m.; though showing signs of uneasiness, she made a pretty good dinner at 2 p.m. Death occurred in thirteen or fourteen hours after administration. This was a French case and very unusual.

A scientific worker in a factory where large quantities of arsenic were used, and where it was impossible to avoid the inhalation and swallowing of a certain amount of arsenic,

told me that sometimes at night, when the exposure to poison during the day had been great, he suffered from vomiting and diarrhoea—that is, there had been a delay of many hours before the onset of the symptoms.

When a poisonous dose is taken in solution on an empty stomach nausea is likely to occur within a few minutes, vomiting within an hour, and diarrhoea within a few hours. A burning pain in the epigastrium is a fairly constant early symptom associated with the nausea and vomiting. A burning pain in the throat has been described as a symptom. This is usually not marked in arsenical poisoning, and then is only caused by the congestion of the pharynx and oesophagus consequent on the vomiting. In a recent case (Black) burning of the throat was a prominent early symptom, occurring apparently before the vomiting and diarrhoea. Arsenic is not a corrosive poison, and no direct local effects are produced on the pharynx or oesophagus, so that it is difficult to explain an immediate burning sensation except by reflex action.

The vomit will at first contain food and mucus, and may later be darkened in colour owing to the exudation of blood from the gastric mucous membrane; afterwards it may be yellowish and slimy owing to the presence of bile and mucus. The diarrhoea may be severe and accompanied by a good deal of abdominal pain and tenderness. The pain is often of a colicky nature and followed by profuse evacuation. The stools are watery, and may contain minute particles of mucus and blood. In suspected cases the vomit and stools should always be carefully reserved for analysis. The tongue is furred in the early stages, and later may have a silvery appearance, the papillae showing through the fur.

In cases of continued doses, as in the Armstrong case, sordes may appear on the lips, as in a typhoid patient. Cramps in the legs are likely to occur when there is severe diarrhoea; where vomiting and diarrhoea are continuous, thirst may become marked owing to the draining from the body of fluid, the eyes sunken, and the face pinched. The appearance of the patient may resemble that seen in cholera, and the examination of the stools, both chemically and bacteriologically, may be necessary to establish the diagnosis.

Cardiac Symptoms.

A weak and rapid pulse is one of the early and most constant symptoms; it was a marked feature in the Black case and also in the Armstrong case (both Mr. Martin and Mrs. Armstrong). The tachycardia is accompanied by weakness, faintness, and a feeling of collapse. There is no doubt that arsenic has a direct toxic action on the cardiac muscle, and this effect is no doubt the cause of the early death in acute cases.

Hepatic Symptoms.

Arsenic is a direct liver poison, and a microscopical examination of the liver in fatal cases of acute arsenical poisoning shows very marked fatty degeneration. Dr. Spilsbury demonstrated this recently in the case of Mrs. Armstrong. One of the most important functions of the liver appears to be that of the protection of the body from circulating poisons. It is the first line of defence, and when the poison is taken by the mouth it is readily to be understood that since after absorption by the portal vein the poison first passes through the liver this organ receives the brunt of the attack and often is irreparably damaged in consequence. The effect on the liver is a degeneration of the cells and in consequence swelling, so that the bile capillaries become pressed upon and slight jaundice may occur. Jaundice is not a common symptom of acute poisoning by arsenious oxide, but it is likely to occur where there have been repeated attacks of poisoning extending over a few weeks. In the case of Mrs. Armstrong one of the nurses (Nurse Kinsey) described the appearance of the skin as being like that of a jaundice case, while the other nurse (Nurse Allen) said the skin was very dark and of a tawny colour.

There is no doubt that the hepatic function is diminished considerably as the result of the action of arsenic, and this accounts for the jaundiced appearance of the skin in protracted cases of arsenical poisoning.

In the Madeline Smith case (1857) Dr. Hugh Thomson, who saw the patient (L'Angelier) during life and who took part in the *post-mortem* examination, described the skin as being of "a distinctly jaundiced hue," both before and after death; in the joint *post-mortem* report of Dr. Thomson and Dr. James Stevens the skin is described as being of a tawny hue. Some discussion arose during the trial as to whether jaundice was due to arsenic, and in the evidence for the defence Dr. MacLagan stated that in arsenical poisoning there

is no jaundice. The victim in the Madeline Smith case probably had three attacks of acute arsenical poisoning during the last five weeks of life—namely, on February 19th and 23rd and March 22nd, the last proving fatal within a few hours. It is now fully recognized that arsenic is a powerful liver poison and so much damage may result that a condition of extensive atrophy (acute yellow atrophy) may follow. The action of arsenobenzol compounds (salvarsan, etc.) on the liver is well known, and in all acute fatal cases where death occurs within two or three weeks of its administration marked fatty degeneration of the liver occurs. Dr. Spilsbury has found this change in several such cases.

It is interesting to note that when the arsenical poison is given into the general blood stream, as in the intravenous administration of arsenobenzol compounds, the liver still acts as the first line of defence against the poison, and in fatal cases the bulk of the poison is found in the liver.

As a consequence of the fatty degeneration of the liver jaundice may occur, and a very large number of cases of salvarsan jaundice have been described. The onset of this symptom is usually late—weeks or months after the administration. As the jaundice clears up usually a definite shrinkage in size of the liver is found, though there is often some swelling present at its onset.

Salvarsan jaundice has been found associated with a defective hepatic function, and in a case under my care at St. Mary's Hospital two months ago the laevulose test for hepatic function, carried out by Dr. Roche Lynch, gave a very marked reaction indicating hepatic deficiency (see chart). Salvarsan jaundice is a serious symptom and not infrequently fatal, the condition of the liver often, at necropsy, showing marked shrinkage due to atrophy following the previous fatty degeneration (acute yellow atrophy).

Liver efficiency test. Case of post-galyl jaundice. X = 50 grams laevulose given.

Renal Symptoms.

Arsenic is a powerful renal poison and acts on the kidney cells, causing fatty degeneration. Impairment of function of the kidney is shown by diminution or even suppression of excretion and the presence of albuminuria.

In the recent Black case albuminuria occurred during life, and fatty degeneration was found in the kidneys on microscopical examination after death. The kidneys also showed definite but not extensive arterio-sclerotic changes which must have been present before the onset of the arsenical poisoning. The action of the arsenic on the damaged kidneys so impaired their function as to be the direct cause of death.

In the Armstrong case albuminuria occurred during the acute illness of Mrs. Armstrong, and fatty degeneration of the kidneys was found by Dr. Spilsbury on microscopical examination. In 1920 a case of subacute arsenical poisoning due to arsenical fruit-spraying liquid was under my care; in this case persistent albuminuria with marked skin lesions occurred and death resulted after a long illness. Probably the lead present in the liquid accentuated the renal symptoms, but undoubtedly the marked albuminuria and other symptoms were mainly arsenical in origin.

Nervous System.

After a single poisonous dose of arsenic, unless this is large, nervous symptoms do not usually occur. Multiple neuritis may follow a single large dose. One instance of this has been described above. Another example came under my notice in Mesopotamia in 1916, where from accident a large quantity of drinking water became contaminated with sodium arsenite. A number of cases of acute arsenical poisoning resulted and in one a most severe arsenical neuritis followed.

In protracted acute arsenical poisoning due to repeated doses, multiple neuritis is a common symptom. It was marked in the case of Mrs. Armstrong, and in the Maybrick case some slight symptoms of neuritis occurred. The brain does not appear to be specially affected in acute arsenical poisoning, and usually the mental condition is unimpaired until a few hours before death.

As will be seen from the analyses of fatal cases, very little arsenic is found in the brain, and the cerebral symptoms in acute arsenical poisoning cannot be due to the direct action

of arsenic on the brain, but to the impairment of function of the other organs (liver, kidneys, and heart) and consequent indirect cerebral toxæmia.

Repeated Doses.

Where repeated doses of arsenic are given, as sometimes happens in criminal cases, symptoms of chronic arsenical poisoning (conjunctivitis, laryngitis, skin rashes and pigmentation—symptoms of multiple neuritis, etc.) may accompany the acute symptoms.

Fatal Dose.

A single dose of 2 grains of arsenious oxide has caused death in a healthy adult, and this is usually accepted as a possible fatal dose. It is common for much larger doses to be taken and recovery occur, owing, no doubt, to the rapid elimination of the poison by vomiting and diarrhoea. A given amount of arsenic if taken in solution and its administration spread over a short period is much more likely to prove fatal than if the whole amount is taken in one dose.

Fatal Period.

It is impossible to state this, since so many factors influence the time of death after a single fatal dose. Usually death occurs within three days, but in cases of repeated dosage death may not occur for many days. In one case after a large dose death occurred in twenty minutes; but in the case already mentioned after a dose estimated at 180 grains death did not occur for three and a half months.

Post-mortem Examination.

In cases where death has occurred some time previously careful search must be made for evidence of delayed putrefaction. This will be best shown by the condition of the internal organs. It is most marked in cases where there has been an illness prolonged over several days, the arsenic being widely distributed throughout the body; the drainage of the tissues consequent on the prolonged diarrhoea and vomiting also tends to delay putrefaction. In a case of illness where the diarrhoea is due to bacterial infection putrefaction will be accelerated, so that in this respect arsenical cases present a marked contrast.

Too much importance, however, must not be attached to delayed putrefaction, and in cases where a single dose only of arsenic has been taken and death has occurred quickly there may not be a marked delay. It depends on many factors—for example, the amount of arsenic distributed throughout the body, and the influence to which the body has been exposed after death, whether favourable or otherwise to putrefactive changes. The presence of inflammatory changes in the stomach and intestine should be carefully looked for, and especially the presence of petechial hæmorrhages. It is important to remember that, as the result of putrefaction, these signs rapidly disappear after death, and it may be quite impossible to detect them when death has occurred many days previously. In a case of exhumation the absence of inflammatory signs in the stomach and intestines is not indicative of the absence of arsenic. The presence of any solid particles of arsenic or of a pigmented powder must be looked for. Where putrefaction is advanced marked yellow staining may be found in the stomach or intestines, due to the formation of arsenic sulphide.

Careful reservation of the organs for analysis and microscopical examination should be carried out. The stomach, the small intestine, the caecum with the ascending colon, and the remainder of the large intestine with the rectum should be separated by ligature and placed in separate jars with due precaution. The contents of these should be kept separate, since the amount of arsenic in each may give an indication of the time of administration of the fatal dose. The liver, kidneys, heart, spleen, and brain should be placed in separate jars. In addition, a portion of muscle, a piece of bone, some hair cut off close to the scalp, a portion of skin, and the nails should be separately reserved in appropriate vessels. Any fluid in the coffin in an exhumation case should be reserved. Also, any earth adherent to the coffin or around it should be reserved for analysis. At the time of the examination small portions of the liver, kidneys, and heart should be placed in normal saline containing 10 per cent. formalin for future microscopical examination.

Chemical Analysis.

Too much importance cannot be attached to the methods employed in the analysis of organs for arsenic in suspected

poison cases. Only those methods should be used which are absolutely reliable and cannot give fallacious results.

As a qualitative test the Reinsch test is one of the most reliable. As a quantitative test where a weighable amount of arsenic is possible, a weighed portion of the organ is taken, the organic matter broken down by the usual method, and the arsenic precipitated as arsenious sulphide by treatment with sulphuretted hydrogen gas, the liquid being kept saturated with the gas for four days. The arsenious sulphide is filtered off, dried, freed from sulphur, and carefully weighed; its purity is confirmed by conversion into magnesium pyroarsenate, which is also weighed.

Where the quantities of arsenic present do not admit of weighing, a known amount of the organ is treated with nitric and sulphuric acids to oxidize the organic matter present. After evaporating off the acids the residue is submitted to the electrolytic Marsh-Berzelius test and the mirror obtained compared with the standard mirrors.

The above tests if carefully carried out are absolutely reliable. It is essential that all reagents should be free from arsenic, and control tests must be constantly done to ensure this. In toxicological work no test should be used which can possibly give fallacious results; for this reason I do not favour the use of the Gutzeit test, though it has been much used in pharmacological work.

The presence of traces of sulphide from putrefaction or of impurities in the chemicals used may lead to error. For the same reason the electrolytic test is to be preferred to the ordinary Marsh-Berzelius test.

It is particularly necessary that most accurate methods be used where only traces of arsenic are present in the material for examination, since the slight mirrors yielded in such cases might be produced by small traces of impurities in the chemicals used.

In toxicological work reliance should not be placed on a single method of testing—thus, if arsenic is found by the Marsh test, its presence should be confirmed by the Reinsch and other tests.

There have been instances in which arsenic has been found in the process of analysis of viscera, and the origin of the arsenic has been traced to the impure chemicals used. A very interesting example of such a mistaken diagnosis came to my notice in 1909.

M. F., a man aged 50, who lived in a large country house in the Midlands, and who was supposed not to have been on the best of terms with his wife, suffered from severe vomiting accompanied by some diarrhoea. The illness had lasted for four weeks, and during this time the wife was frequently in and out of the sick-room.

The patient had been addicted to alcohol for years, and even during his last illness took a fair amount of whisky, though not in great excess. The patient died, but before his death some suspicion rested on the wife, and in consequence the urine was collected and sent to a local pharmacist for analysis. The manner of collection of the urine was open to suspicion, and no especial care was taken as regards the cleanliness of the bottle or cork used. The urine was analysed by the Marsh test and a very large mirror of arsenic resulted. This mirror was much larger than would have been given by urine passed by a patient who had recently received a fatal dose of arsenic, and this of itself aroused my suspicions as to the danger of drawing any conclusions whatever from this piece of evidence. The presence of arsenic in the urine had not been confirmed by the Reinsch or other tests. The death of the patient resulted within two days of the collection of the sample of urine.

A post-mortem examination was made, and the organs were examined and analysed by me. The liver was greatly increased in size and of canary-yellow colour; microscopical examination showed that the cells were engorged with fat. No trace of arsenic was present in the liver or any of the organs of the body. The liver was in a state of very marked fatty cirrhosis due to alcohol, a condition commonly associated with most severe vomiting and a certain amount of looseness of the bowels. It is also commonly associated with symptoms of peripheral neuritis due to alcohol, and a fatal termination is by no means uncommon. The clinical picture is almost exactly like that of arsenical poisoning, and in the case of M. F., where arsenic was said to have been found in the urine in large quantity, it was not surprising that a confident diagnosis had been made of acute arsenical poisoning, and that a sensational second Maybrick case was supposed to have arisen.

The fact that all the organs of the body were free from arsenic at the time of death, even though submitted to the delicate Marsh-Berzelius test, showed conclusively that the urine passed two days before death must have been free from arsenic, since had it contained arsenic as suggested considerable amounts must have been present in the liver and other organs.

It was clear that the arsenical mirror obtained on the analysis of the urine had come from some extraneous source, either from a dirty bottle or from impurities in the chemicals used in the analysis. The facts of the case were carefully explained to the jury, and a verdict of death from cirrhosis of the liver was found.

This case was an excellent illustration of the ease with which a mistaken diagnosis of arsenical poisoning may be

made. It also emphasizes the necessity of taking the utmost care in analysis and collection of specimens, and the importance of relying neither on one test nor on the results of analysis of one organ.

In a fatal case of arsenical poisoning arsenic should be found in the liver, spleen, kidneys, and other organs of the body, in addition to being present in the gastro-intestinal tract.

Elimination of Arsenic.

In acute arsenical poisoning the vomit and faeces will contain arsenic in amount depending on the quantity of the poison taken. The absorbed arsenic will be found in the blood and serous exudations.

Thus in one case the blood collected one hour after the injection of 0.6 gram of salvarsan contained 0.5 mg. and in another 0.33 mg. per 100 c.cm. The blood will contain traces of arsenic as long as the poison is present in the liver and organs; in fatal cases the blood and serous exudations contain appreciable amounts of arsenic. The urine after the administration of arsenic will contain arsenic for several days. After medicinal dosage, usually at the end of fourteen days, arsenic cannot be detected in the urine, but I have found definite evidence of arsenic twenty-one days after the administration of a single dose of salvarsan (0.5 gram). Where repeated doses of an arsenobenzol preparation have been given arsenic may probably be found in the urine for several weeks or even months.

Dr. Chalmers Watson recorded a case in the *Lancet*, April 22nd, 1922, where traces of arsenic were found in the urine and faeces fifteen months after a course of ten injections of novarsenobenzol, and Dr. D. R. C. Shepherd recorded a case in the *Lancet*, December 17th, 1921, where arsenic was found in the urine 111 days after a course of seven injections of neo-salvarsan. In the beer poisoning epidemic arsenic was found in the urine by Dr. Dixon Mann in one instance fifty-nine days after admission of the patient to hospital.

It is probable that during the prolonged administration of arsenic a certain amount becomes deposited in the skin, hair, and nails, and that this is gradually reabsorbed, being excreted by the urine and faeces; hence the poison may be found for long periods after the administration. Usually in acute arsenical poisoning after a single dose arsenic ceases to be found in the urine and faeces after about three weeks. The late Dr. Dixon Mann, who had a very extensive experience of the toxicology of arsenic, wrote in his textbook:

"In cases of acute arsenical poisoning it is very exceptional to find arsenic in the urine longer than a week or ten days after the administration of the poison; and in those fatal cases in which the patient survived more than ten days arsenic has rarely been found in the tissues."

I believe from my own experience that this still holds true in the majority of cases of acute arsenical poisoning arising from the taking of a single dose by the mouth.

Arsenic has a strong affinity for the keratin tissues, and hence it is found in the hair, nails, and skin, especially in cases of prolonged administration. In the hair it is deposited in proximal portions which represent the growth during the period absorbed arsenic is in the body. The sweat and sebaceous secretion during this period will contain arsenic, and as the whole length of the hair comes in contact with these secretions the limitation of arsenic to the proximal portions of the hair is relative not absolute. The analyses in the Armstrong case illustrated this point. In the Seddon case Sir Edward Marshall Hall quite rightly raised the question of why arsenic should be present in the distal portions of the hair if the case was one of acute poisoning as suggested. In this case the distal hair had been lying in blood-stained fluid in the coffin, and as this fluid contained definite traces of arsenic I gave it as my opinion that the arsenic in the distal portions of the hair had been absorbed from the fluid in the coffin. The accuracy of this statement was confirmed by soaking some arsenic-free hair in the blood-stained arsenical fluid for twenty-four hours and then thoroughly washing it in water, alcohol, and ether, and submitting it to analysis. It was found that an appreciable amount of arsenic had been absorbed by the hair, thus explaining the presence of arsenic in the distal portion of the hair from the deceased.

Arsenic may be found in the sweat, saliva, and bronchial secretion in acute arsenical poisoning, and it has also been found in the milk of lactating women. In two cases where salvarsan was given to patients during lactation I found arsenic to be absent in samples of milk taken from five and

a half to seventy-two hours after the administration, so that the benefit to the child resulting from the administration of salvarsan to the mother cannot be due to the presence of arsenic in the milk but to other causes.

TABLE I.

Patient E. M. Has taken liq. arsenicalis m 3 t.d.s. from November 28th to December 25th; m 5 t.d.s. from December 25th to January 1st inclusive; m 7 t.d.s. from January 4th to January 8th inclusive. All specimens were collected from 8 a.m. to 8 a.m.

Specimen.	Urine.		Faeces.	
	Amount of As per 100 c.cm. of Urine.	Total As in 24 hours Specimen.	Amount per 100 grams.	Total Amount in 24 hours.
January 5-6 ...	Mg. 0.095	Mg. 0.95	B.N.O.	Mg. —
" 6-7 ...	0.48	4.01	*1.0 mg.	0.5
" 7-8 ...	0.11	2.96	B.N.O.	—
" 8-9 ...	0.09	1.1	*0.9 mg.	0.45
" 9-10 ..	0.10	0.58	0.30 ..	0.46
" 10-11 ...	0.04	0.32	B.N.O.	—
" 11-12 ...	0.03	0.26	0.4 mg.	2.6
" 12-13 ...	0.04	0.31	*0.05 ..	0.025
" 13-14 ...	0.02	0.24	0.045 mg.	0.09
" 14-15 ...	0.01	0.10	Trace too small to estimate	
" 15-16 ...	0.001	0.01		
" 16-17 ...	nil	nil		

* The total amount of faeces was about 50 grams.
B.N.O. = Bowels not opened—no specimen.

TABLE II.

Patient H. H. Has taken liq. arsenicalis m 3 t.d.s. from January 4th to 10th inclusive.

Specimen.	Urine.		Faeces.	
	Amount of As per 100 c.cm. of Urine.	Total As in 24 hours Specimen.	Amount per 100 grams.	Total Amount in 24 hours.
January 7-8 ...	Mg. 0.06	Mg. 0.4	B.N.O.	Mg. —
" 8-9 ...	0.05	0.26	0.08 mg.	0.55
" 9-10 ...	0.14	0.83	0.09 ..	0.38
" 10-11 ...	0.07	0.69	B.N.O.	—
" 11-12 ...	0.03	0.17	0.069 mg.	0.69
" 12-13 ...	0.035	0.22	B.N.O.	—
" 13-14 ...	0.04	0.24	0.03 mg.	0.08
" 14-15 ...	0.003	0.022	0.016 ..	0.025
" 15-16 ...	0.002	0.014	0.003 ..	0.013
" 16-17 ...	Less than 0.001	0.005	Not estimated.	

The accompanying tables of cases investigated personally illustrate the excretion of arsenic by the urine and faeces.

TABLE III.—Excretion of Arsenic.

Case 1.—P. L. June 2nd, 1914; 0.6 gram salvarsan given.

Milligrams of arsenic (As ₂ O ₃) per 100 grams.				
	Urine.		Faeces.	
June 3rd ...	1.0	...	1.4	...
June 5th ...	1.0	...	2.5	...
June 7th ...	0.17	...	1.7	...
June 9th ...	0.17	...	—	...
June 10th ...	0.07	...	—	...

TABLE IV.—Excretion of Arsenic.

Case 2.—H. October 12th, 1914; 0.5 gram salvarsan given.

No. of days after salvarsan.	Mg. of As ₂ O ₃ in 100 c.cm. urine.
4 ...	0.3
7 ...	0.3
10 ...	0.15
13 ...	0.03

TABLE V.—*Excretion of Arsenic.*

Case 4.—October 29th, 1914; 0.5 gram salvarsan given.

No. of days after salvarsan.	Mg. of As ₂ O ₃ in 100 c.cm. urine.
4	0.4
7	0.4
10	0.2
13	0.1
16	0.03
21	0.025

TABLE VI.—*Excretion of Arsenic.*

Case 6.—F. October 12th, 1912; 0.5 gram salvarsan given.

No. of days after salvarsan.	Mg. of As ₂ O ₃ in 10) c.cm. urine.
2	1.33
4	0.4
7	0.16
10	0.11
13	0.025

Distribution of Arsenic in the Body in Fatal Cases.

This is well illustrated by the accompanying tables (VII to XIII). No rule can be laid down for the exact proportion of arsenic found in the various organs, since this will depend on the mode of administration, whether in one or repeated doses, on the time that has elapsed since the last dose, and on the state of health of the patient at the time of administration. The distribution of arsenic along the alimentary canal is of great importance because it gives a definite indication of the time at which the last dose was administered.

The routine examination of the alimentary tract by *x* rays after an opaque meal has given us definite knowledge of the rate of passage of the gastro-intestinal contents. Thus after twenty-four hours the bulk of the arsenic will have passed through the gastro-intestinal tract, as illustrated by the three Bingham cases. In the Armstrong case the large amount of arsenic in the caecum showed that a poisonous dose had been taken within twenty-four hours of death.

The liver, as has already been mentioned, rapidly absorbs arsenic, and usually considerable amounts are found in it, as is shown by the Armstrong and three Bingham analyses. In the Seddon case the amount was relatively small, while the amount in the muscles was high, probably owing to there having been a break in the repeated dosage. The large amount found in the intestines showed that a dose had been given within twenty-four hours of death.

Arsenic is usually found widely distributed through all the organs. The brain, however, contains only very small amounts, and I have found this to hold good, not only for poisoning by inorganic arsenic, but also for the organic arsenobenzol compounds. Stevenson and Dixon Mann had a like experience. This explains the absence of cerebral symptoms in acute poisoning by inorganic arsenic, and also shows that

TABLE VII.—*Distribution of Arsenic.*

Maybrick Case.

	Grains.	Milligrams.
Stomach	nil	nil
Intestines	1/11	6
Kidneys	trace	trace
Liver	0.3	21
Total	43/100	27

TABLE VIII.—*Distribution of Arsenic.*

Rex v. Bingham. Re Margaret Bingham (deceased). Death in three or four days from onset.

Stomach	1/250 grain
Liver	1.1 grain
Kidneys	1/130 grain
Spleen	trace

TABLE IX.—*Distribution of Arsenic.*

Rex v. Bingham. Re James Bingham (deceased). Onset August 12th, 1911, 3 p.m.; death August 15th, 1911, evening.

Stomach	minute traces
Liver	1/2 grain
Kidneys	1/95 grain
Spleen	1/600 grain

TABLE X.—*Distribution of Arsenic.*

Rex v. Bingham. Re William Hodgson Bingham (deceased). Onset January 22nd; death January 24th, early morning. Duration 23 hours, about.

Stomach	1/12 grain
Small intestine	1/40 grain
Liver	1 grain
Kidneys	1/250 grain
Spleen	1/500 grain

TABLE XI.—*Distribution of Arsenic.*

Seddon Case.

	Grains.	Milligrams.
Stomach	0.11	7.30
Intestine	0.63	41.00
Liver	0.17	11.13
Kidneys	0.03	1.91
Spleen	0.007	0.44
Lungs	0.014	0.94
Heart	0.012	0.80
Brain	0.005	0.33
Blood (fluid from chest)	0.006	0.38
Bone	trace	trace
Nails	0.002	0.14
Skin (0.18 mg. per 100 grams)		
Muscle	1.03	67.20
Hair—proximal (3 mg. per 100 grams)		
Total	2.01	131.57

TABLE XII.—*Distribution of Arsenic.*

Rex v. Greenwood. Re Mrs. Greenwood (deceased).

	Grains.	Milligrams.
Stomach	0.009	0.6
Small intestine	0.067	4.33
Large intestine	0.008	0.55
Rectum	0.006	0.40
Liver	0.131	8.5
Spleen	0.006	0.4
Kidneys	0.019	1.21
Uterus	0.012	0.75
Heart	0.004	0.27
Lungs	0.012	0.79
Oesophagus	0.003	0.21
Brain	0.001	0.09
Total	0.23	18.07

TABLE XIII.—*Distribution of Arsenic.*

Rex v. Armstrong. Re Mrs. Armstrong, deceased.

	Milligrams.
Stomach	2.5
Stomach contents	2.0
Jejunum and contents	1.6
Ileum and contents	9.1
Caecum, ascending colon, and contents	37.6
Liver	138.0
Spleen	1.0
Kidneys	13.2
Left lung	0.5
Heart	0.6
Fluid from pleural cavities	0.9
Portion of brain (14 oz.)	0.1
Bone from left femur (4 oz.)	0.01
Skin from left thigh (3½ oz.)	0.25
Muscle, back of left thigh (3½ oz.)	0.21
Hair from head (3½ oz.)	0.54
Finger-nails	0.06
Toe-nails	0.03
Total	208.2

the cerebral symptoms in acute salvarsan poisoning are due to auto-intoxication and not to the direct action of arsenic on the brain. In acute arsenical poisoning very little arsenic is found in the bone, as illustrated by the Seddon and Armstrong cases.

Poisoning by Arsenobenzol Derivatives.

This subject has been dealt with by me in a paper published in the BRITISH MEDICAL JOURNAL, April 1st, 1916. The interest attaching to cases of acute poisoning by salvarsan and allied compounds is that here, instead of gastro-intestinal symptoms occupying the prominent position, it is the poisonous effects of the arsenical compound on the organs of the body which produce the fatal symptoms. The liver bears the brunt of the attack and is the organ to suffer most damage. In fatal acute cases marked fatty degeneration is found in the liver, and the kidneys and heart muscle also commonly show this change.

The symptoms of acute salvarsan poisoning exactly simulate those of icterus gravis, and they are in my opinion due to auto-intoxication from defective liver function consequent on the action of the poison on the liver cells.

Very extensive damage and impairment of function is necessary for fatal auto-intoxication to be produced, but these cases do occur, and the risk from salvarsan administration should always be borne in mind. Even when the poisonous effect of salvarsan is not so massive, yet in many cases the liver suffers from the effect of repeated doses, and this is proved conclusively by the frequent occurrence of jaundice due to liver damage. This jaundice may occur weeks or months after salvarsan administration and may be most serious.

I am of opinion that the toxic action of salvarsan compounds on the liver is not sufficiently borne in mind in the very extensive use of this drug at the present day. Professor Maclean has suggested that liver damage is less likely to follow salvarsan administration if the liver cells have stored in them a certain amount of glycogen, and he has recommended that danger may be avoided by taking glucose shortly before the drug is given. This precaution is undoubtedly of value, and it has been emphasized by the use of a drug having like effects on the liver—namely, chloroform in its production of delayed chloroform poisoning after anaesthesia.

I wish to express my sincere thanks to Mr. J. Webster and Dr. Roche Lynch for valuable and much appreciated help in the work connected with this paper.

THE BLOOD SERUM IN PERNICIOUS ANAEMIA.

WITH NOTES ON THE NATURE OF THE DISEASE AND ITS TREATMENT.

A Preliminary Note.

BY

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Two years and a half ago, when making some observations on the phosphorus content of the corpuscles, clot, serum, and plasma of pernicious and other anaemias, I noticed that the colour of the plasma or serum of pernicious anaemia differed from that seen in the plasma or serum of any other anaemia or of normal blood. Since making the observation I have used it regularly in the diagnosis of pernicious anaemia and have found it a most useful and reliable, if not a pathognomonic, test of this anaemia.

By pernicious anaemia I mean a severe anaemia of unknown cause with high colour index, almost always above normal; urobilinuria; a tendency to megaloblast formation, and leucopenia; absence or great scarcity of blood plates (as seen on smears); and, judging from observations which are recorded in this paper, serum and plasma with special characteristics.

The serum in pernicious anaemia is always of a definite yellow colour, varying in tint from that of a cowslip to the deeper buttercup yellow of Canada balsam, whilst the serum of all other anaemias is much paler, and resembles straw-coloured water. The yellow colour is so distinct that it can be recognized in the serum or plasma if only two or three drops of blood are drawn into, and half fill, a small bulb made of thin glass with inlet and outlet of a narrow bore which can be closed hermetically by sealing-wax. Care must be taken not to heat the glass bulb and blood with the wax, for this would tend to haemolyse the blood; it is for this reason that sealing the ends of the bulb with heat is risky. For the past two years I have regularly carried these glass bulbs about with my blood slides, and used one in each case of anaemia examined. The blood runs freely into the small bulb from a needle puncture (when it is held lower than the blood drop on the finger), and when the ends of the bulb are sealed I stand it upright, or if taken at a patient's house I carry it upright in a small box in a waistcoat pocket until serum and clot separate. The colour of the serum is then seen, and, judging from a score or more of cases of pernicious anaemia and twice the number of other anaemias—Banti's disease, the leukaemias, secondary anaemia from any cause, purpura haemorrhagica—a diagnosis of pernicious anaemia from any other anaemia can be made. I have not applied the test to the anaemia of intestinal parasites which simulates pernicious anaemia, as I have never had any case of the condition under my care. A very important point is that serum from cases of severe secondary anaemia is pale straw colour, not yellow, in all the cases I have tried, whether due to septic infection, haemorrhage, or concealed malignant disease, which all have a high colour index (though not above 0.9) and a microscopic red blood cell appearance simulating pernicious anaemia but with leucocytosis. The blood in these severe secondary anaemias is specially referred to in the diagnosis of pernicious anaemia by Gulland and Goodall.¹

case of anaemia examined. The blood runs freely into the small bulb from a needle puncture (when it is held lower than the blood drop on the finger), and when the ends of the bulb are sealed I stand it upright, or if taken at a patient's house I carry it upright in a small box in a waistcoat pocket until serum and clot separate. The colour of the serum is then seen, and, judging from a score or more of cases of pernicious anaemia and twice the number of other anaemias—Banti's disease, the leukaemias, secondary anaemia from any cause, purpura haemorrhagica—a diagnosis of pernicious anaemia from any other anaemia can be made. I have not applied the test to the anaemia of intestinal parasites which simulates pernicious anaemia, as I have never had any case of the condition under my care. A very important point is that serum from cases of severe secondary anaemia is pale straw colour, not yellow, in all the cases I have tried, whether due to septic infection, haemorrhage, or concealed malignant disease, which all have a high colour index (though not above 0.9) and a microscopic red blood cell appearance simulating pernicious anaemia but with leucocytosis. The blood in these severe secondary anaemias is specially referred to in the diagnosis of pernicious anaemia by Gulland and Goodall.¹

This serum bulb test is very simple and has been a most useful aid to me many times in the diagnosis of the type of anaemia under investigation. In its average appearance I can tell from the serum alone, and without the estimation of the colour index or an examination of the blood film, whether I am dealing with a case of pernicious anaemia; but, of course, I always make and examine a blood smear, and wherever possible estimate the colour index as well. On some occasions I have had my clinical opinion of a case confirmed or altered on my way home in a train by the colour of the serum which has separated from the clot.

There is no question of any pink colour in the deeper coloured yellow serum—nothing whatever to suggest the presence of any trace of haemoglobin or haemolysis; nor is it of a bile pigment tint.

In taking larger amounts of blood from a vein haemolysis is liable to occur in health or disease if there is any trace of alcohol or distilled water in the syringe or needle. This is avoided by drawing 0.5 c.cm. of sterile 5 per cent. sodium citrate solution through the sterilized needle into the sterilized syringe, and withdrawing the piston to its full extent, thus rinsing the barrel of the syringe with the citrate solution, which is then expelled from the syringe. The needle is then put into the vein, and blood withdrawn. Finally, the blood is expelled gently into a sterile test tube, which is handled very gently and laid down in a sloping position to facilitate separation of clot and serum. The serum is pipetted away from clot without disturbing red corpuscles and then well spun in a centrifuge.

Every precaution is taken to avoid haemolysis. Some of my specimens were taken with dry Wassermann outfit needles direct into a dry sterile test tube without any syringe; some were taken with an oiled syringe by Dr. Loveday, who has been director of our clinical laboratory for many years, and is thoroughly experienced in the dangers of haemolysis and the methods of avoiding it.

At first I could find no reference to the colour of the serum in pernicious anaemia in textbooks of medicine and pathology or monographs on blood diseases. There is no mention of it in Hunter's monograph, in French's full article on pernicious anaemia in Allbutt's *System of Medicine*, or in Gulland and Goodall's book on the blood. In the last named work a suggestion that the increased haemoglobin index may be accounted for by the presence of haemoglobin in the serum is mentioned, but no evidence is advanced in support of it.

In the section by Lazarus (p. 20) on the clinical methods of blood investigation in *Die Anaemie* (Ehrlich, 1909) there is no reference to the colour of the serum. The only mention of it that I have been able to find is in Panton's *Clinical Pathology*, where it is said:

"The bile colour of some serums is more closely simulated by the greenish-yellow pigment present in the serum of nearly all cases of pernicious anaemia. A certain percentage of these cases are, in addition, actually jaundiced."

In none of my cases of pernicious anaemia has the serum had a greenish tint.

Cause of the Colour of the Serum.

A larger amount of serum than that obtained in the bulbs is necessary to make any observations on the cause of the colour; for this purpose 5 c.cm. of blood or more are withdrawn from a vein in the arm with the precautions already referred to. The colour of the blood serum and plasma in pernicious anaemia calls to mind the striking yellow colour of the fat in the body, and the question of any possible connexion between the two and of the colouring matter being a lipochrome naturally arises. There is also the possibility of the presence of some bile pigment in the serum even in cases in which there was no real jaundice. I therefore examined the serum with the spectroscope—using a simple pocket or straight vision instrument—and immediately saw two very distinct absorption bands in the position of those of oxyhaemoglobin, and a much less distinct narrow third band farther to the right in the green in some specimens. These absorption bands appeared in all the specimens of pernicious anaemia serum or plasma examined except the very pale ones. This difference may be due possibly to the small quantity used, but possibly, as I believe, to there being more than one form of the disease. In the deeper coloured serum the bands are very distinct when the depth of fluid is only one-third of an inch and the shadows are about the same intensity as those of oxyhaemoglobin in 0.01 per cent. solution as depicted in Starling's *Textbook of Physiology*. I never saw any bands to the left of the D line in the red. In normal serum and