tor in determining the presence or degree of mental defect. Conduct, and in practice this implies an accurate history of the patient from an early age, is still the best intelligence test at our disposal, and it should be remembered that the slighter the degree of defect the greater will be the age at which conduct and behaviour begin to show evidence of abnormality.

TOXICOLOGY IN ITS APPLICATION TO MEDICAL PRACTICE.

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"THE HARVEIAN LECTURE" DELIVERED BEFORE THE HARVEIAN SOCIETY, ON THURSDAY, MARCH 15, 1928.

THE Harveian Lectures of the Harveian Society were instituted in 1875, in which year the first lecture was given by Dr. Sibson, F.R.S., "On Bright's Disease and its Treatment: Considered mainly in Relation with Arterial Tension from Blood Contamination."

Harveian Lectures have since that date been given annually by members of the medical profession selected by the Council of the Harveian Society. The list includes the honoured names of many of the well-known leaders of the medical profession of their day, and the titles of the lectures include a wide diversity of most important subjects in medical science.

Toxicology has not yet formed one of the subjects of the lectures and it is therefore fitting that the fifty-fourth lecture should be devoted to this branch of medicine.

Toxicology has, from the earliest times, been a branch of medicine which has had a fascinating attraction, for it deals with the action of poisons on the body, and sometimes the toxicologist has been called upon to unravel the hidden mystery of the cause of death in some famous criminal trial.

Toxicology has always been a very important branch of medicine because of its relationship to the legal aspects of medicine, and it will always retain this position.

In modern times, toxicology has attained a position of the utmost importance in its relationship to medicine, and has become so closely interwoven with scientific medicine as to form an intimate and inseparable part.

The studies of Pasteur in 1860 formed the foundation of bacteriology, and the development of this branch of pathology has elucidated the cause of many diseases.

It is now recognized that the symptoms of disease are usually due to the development of toxins or poisons in the body. These poisons are in some cases produced by the entrance into the body of germs from without which by their growth produce toxins, as occurs in pathogenic diseases such as typhoid, tuberculosis, diphtheria, &c., where the invading causal organism is known.

In recent years, the development of the theory of "focal infection" has shown that an important factor in the causation of many pathological conditions, such as chronic rheumatism, gastric and duodenal ulceration, diabetes, &c., is the production of toxins or poisons in the body at some localized focus, such as infected teeth, septic tonsils, infected nasal sinuses, &c.

These toxins, by their distribution into the circulation, may set up some disease in parts of the body far distant from the originating focus of infection.

In other cases, owing to impairment of the function of organs which are of importance in the body economy either for excreting toxic substances or for regulating its metabolism, toxins are produced which give rise to symptoms known as auto-intoxication.

Examples of this are the symptoms of uræmia produced by defective renal action, or the symptoms of auto-intoxication resulting from impaired function of other organs, such as the liver, suprarenal glands, pancreas, &c.

The study of the action of the toxins in conditions of auto-intoxication, whether of internal or external origin, is still in its infancy, and little is known of the nature of the chemical constitution of the actual poisons giving rise to such conditions as uræmia, eclampsia, icterus gravis, &c.

Toxicological researches on these lines will do much to advance our knowledge of the causation of disease, and should throw light on methods for prevention and cure.

Pharmacology and toxicology are most closely related. The therapeutic action of a drug merges insensibly into a toxic action, and the dividing line between them varies for different individuals owing to idiosyncrasy, and possible variations in tolerance, due possibly to defective function of kidney, liver, or other organ.

In former years where the use of drugs was limited to remedies, the action of which was known from long experience, and where the mode of administration was mainly oral, it was uncommon for toxic symptoms to arise as a result of medical treatment.

Minor troubles might arise from such occurrences as:—

Bromide administration, where a troublesome acneiform rash might develop.

Iodides may give rise to a rash of acneiform type with occasionally larger bullous lesions or even purpura. The rash is often associated with a metallic salty taste and with an irritating catarrh of the naso-pharynx.

Belladonna preparations might give rise to dryness of the mouth, impairment of vision due to pupil paralysis, or to difficulty in passing water owing to temporary retention from action on the nervous mechanism of micturition.

Salicylates and salicylic acid preparations might give rise to deafness or vertigo, and occasionally to cardiac disturbances such as faintness, and tachycardia in persons possessing an idiosyncrasy. Symptoms of acidosis, such as nausea, vomiting, air hunger, delirium, twitchings, or even convulsions and fatal coma might follow large doses,

and these were associated with the presence of acetone and diacetic acid in the urine. The possible danger of acidosis has led to the modern custom of always combining salicylates with alkali-producing drugs such as the bicarbonate or citrate of sodium or potassium. Symptoms of acidosis are dangerous and call for the immediate cessation of the drug.

Mercurial preparations when pushed as in the treatment of syphilis, &c., might give rise to offensive breath, furred tongue, salivation, stomatitis, looseness of the teeth, diarrhoea, and even ulcerative colitis. One rarely sees these symptoms at the present day owing to the replacement of mercurial preparations by other remedies. It is well to remember that they may sometimes follow the continued daily use of small doses of calomel, a method of treatment sometimes adopted in abdominal conditions.

Opium preparations have been long recognized as requiring great care in their use. Their increased toxic effects in the young, and their toxic action in patients with defective renal or hepatic function always demand most careful consideration.

Quinine may give rise to unpleasant symptoms such as headache, deafness, noises in the ear, vertigo, &c., which are not of dangerous import and may often be controlled by the use of bromides.

In rare cases a special idiosyncrasy exists for a specific action of quinine on the retina. Partial or complete blindness may follow even small doses of quinine and this may be associated with retinal changes and even optic atrophy. I have seen almost complete amaurosis follow two doses of 10 gr. of quinine in twelve hours by the mouth in a case of malaria. In such cases quinine must be avoided entirely.

MODERN PHARMACOLOGY.

In the treatment of many diseases at the present time the administration of large doses of drugs possessing powerful therapeutic action is advocated. In many

instances these remedies are given intravenously.

The studies of Ehrlich in his researches for a remedy which would have a selective toxic action on the invading microbe and would not be harmful to the host, led to the trial of various organic compounds of arsenic.

Atoxyl which was first tried was abandoned because of its affinity for the optic nerve and the occurrence of optic atrophy following its use.

After further research salvarsan (Di-oxy-di-amido-arseno benzol dihydrochloride) was discovered in 1910. A modification, "Neo Salvarsan," was shortly afterwards introduced (in 1912), this compound having some advantages for convenience of administration. Since that time innumerable arseno-benzol derivatives have been introduced, but none of them has proved superior in therapeutic value to the original salvarsan, though many of the new preparations possess facilities for administration.

Ehrlich's discovery was one of the greatest therapeutic advances of modern times. Arseno-benzol compounds have become definitely established as the most effective remedy for the treatment of syphilis and they have proved of great value in the treatment of other diseases, especially those due to spirochaetal infections such as relapsing fever, yaws, spirillosis of birds. They have also been of value in the treatment of tertian malaria and other tropical diseases.

Ehrlich's idea was to give a full dose of the arseno-benzol compound (*magna therapia sterilisans*) so as to obtain the greatest therapeutic effect possible without serious harm to the patient.

Even with the greatest care slight toxic symptoms commonly follow the administration of salvarsan in full dose, thus nausea, slight diarrhoea, slight albuminuria, and a slight rise of temperature lasting from twelve to twenty-four hours are common after-effects which disappear in a day or two.

At the present time strict supervision is exercised over all the arseno-benzol preparations used in this country. All have to be passed by the Medical Research Council. Any batches showing evidence of impurity or increased toxicity are rejected.

In spite of the utmost care occasionally serious or even fatal symptoms will follow arseno-benzol administration. The drug has a toxic action on the liver, and in some cases partial or even complete suppression of liver function has occurred after its use. Jaundice may occur as the result of the hepatitis which sometimes follows the administration. It may occur within three or four days, or be deferred for several weeks.

Skin rashes of obstinate type occasionally follow arseno-benzol therapy.

The common symptoms of acute arsenical poisoning such as vomiting, diarrhoea, neuritis, &c., do not usually follow arseno-benzol.

The mode of introduction of salvarsan to the medical profession by Ehrlich was a model of perfection. He delayed the introduction until after repeated preliminary trials on human beings. He gave the fullest warning of possible dangers from its use and pointed out the contra-indications for use, such as renal, brain or hepatic disease.

The use of arseno-benzol compounds in the treatment of syphilis has been followed by the use of various preparations of bismuth by intramuscular injection. These are by no means free from toxic effects, and I have known of cases where severe cerebral symptoms, such as convulsions and coma, have followed their use.

Tropical diseases, such as trypanosomiasis, kala-azar, &c., have called for the use of powerful remedies, and organic compounds of antimony, such as stibosan, stibenyl, tartar emetic, sodium antimony, tartrate, &c., have been used intravenously with marked curative value. These compounds appear to have a selective action on the invading organism. They may give rise to toxic

symptoms, such as vomiting, diarrhoea and hepatic disturbance. Great care is required in order to avoid toxic effects.

The lead treatment for cancer, recently introduced by Professor Blair Bell, is an example of the careful use of a poisonous metal so as to obtain the full therapeutic effect without the production of serious toxic symptoms.

Intravenous injections of colloidal lead 0.5 per cent., or colloidal lead selenide 0.2 per cent., are used, and the injections are repeated at intervals of a week or so over a period of several months until a total amount of about 0.5 grm. is given.

It is desired to produce a therapeutic effect on the cancer cells without damage to the healthy tissues of the body.

Much light has been thrown on the toxicology of lead by its use in this manner, and it is of interest to note that the effects following the intravenous use of lead under proper control differ considerably from the toxic results which occur in chronic lead poisoning where the poison is absorbed by the gastro-intestinal tract. In the latter condition the cardio-vascular system, kidneys and nervous system usually suffer damage from chronic disease, while these effects are not specially noticeable after the therapeutic use of lead intravenously.

LIVER POISONS.

When poisons are absorbed into the blood-stream, by whatever means, whether by the gastro-intestinal tract, the respiratory system (as in the case of general anaesthesia), or by intravenous, intramuscular, or hypodermic injection, the liver is the first line of defence. The liver has the property of acting like a retention filter and absorbing the poison.

This is proved by the toxicological analysis of the various organs of the body when death occurs within a few days of the administration of the poison. In such cases a large proportion of the absorbed poison will be found in the liver. I have repeatedly

found this to be so in cases of arsenical poisoning whether the poison has been taken by the mouth as an inorganic preparation or whether it has been administered intravenously as in arseno-benzol treatment. In morphine poisoning the bulk of the alkaloid is found in the liver, and before death the morphine is gradually excreted from the liver into the stomach. In the case of fatal poisoning by other alkaloids a large proportion of the absorbed poison is found in the liver.

After poisoning by metallic poisons, such as compounds of lead or mercury, or after organic poisons, such as chloroform, tetrachlor-ethane, barbituric acid derivatives, phenol, tri-nitro-toluene, &c., a large proportion of the absorbed poison is found in the liver.

This function of the liver, in protecting the body from exogenous poisons, whether chemical, bacterial, or protozoan, has not been sufficiently realized. In 1922, at the Annual Meeting of the British Medical Association, in the "Discussion on Degenerative Diseases of the Liver," I suggested the term "toxiphylactic function" as a suitable description.

It cannot be claimed that the liver stands alone in possessing this function, because the spleen, kidneys, and other tissues of the body have the property of retaining absorbed poisons, but to a much less extent than the liver. In the exercise of its toxiphylactic function the liver cells suffer damage, and cloudy swelling, fatty degeneration, and even death of the cells often result.

In many cases the liver may truly be said to have laid down its life in its endeavour to protect the body from the action of exogenous poisons.

For example, in phosphorus poisoning, the liver cells may become almost entirely destroyed. In cases of acute fatal poisoning by salvarsan, tetra-chlor-ethane, tri-nitro-toluene, chloroform, &c., such extensive fatty degeneration of the liver cells is found as to make it clear that the normal function of

the liver in the body metabolism must have been almost entirely destroyed. In such cases the real mode of death is an auto-intoxication due to loss of liver function rather than a direct action of the poison in question. It is not only chemical poisons which cause damage to the liver cells. Exactly the same result may follow the action of bacterial toxins, such as in the jaundice of typhoid and paratyphoid fevers, influenza, pneumonia and streptococcal infections.

A similar result may be produced by the toxins in protozoal infections, such as syphilis, yellow fever, kala-azar, malaria, amœbic dysentery or spirochætosis ictero-hæmorrhagica.

In auto-intoxication such as uræmia and recurrent vomiting, the same liver changes may occur.

Examples of chemical poisons having a special action on the liver are :—

Tetra-chlor-ethane, which was used as one of the constituents of a cellulose solvent for the varnish used on aeroplane wings in the early stages of the war. The vapour gave rise to a large number of cases of toxic jaundice among aeroplane workers.

Chloroform, delayed chloroform poisoning which may occur within two or three days of the use of the chloroform as an anæsthetic.

Tri-nitro-toluene, a commonly used explosive during the war caused many cases of toxic jaundice amongst munition workers.

Phosphorus, toluylene diamine, phenyl hydrazine, dinitro benzene, dinitro phenol, arseniuretted hydrogen, inorganic compounds of arsenic and antimony.

The arseno-benzol compounds have been already referred to.

Quinoline derivatives have been found in several instances to act as liver poisons and to give rise to fatal toxic jaundice. Examples of these in common use are the preparations known as atophan, atoquinol and atophanyl.

In July and August, 1926, letters appeared in the *British Medical Journal* from Dr.

Langdon Brown, Dr. Geoffrey Evans, Dr. Worster-Drought and myself calling attention to the occurrence of toxic jaundice after the use of these preparations.

As recently as March 8, 1928, there was an account of the inquest at Southport on a woman, aged 55, who died from acute yellow atrophy of the liver following the therapeutic use of atophan. There can be no doubt that in some cases the quinoline derivatives act as powerful liver poisons, and their use should be avoided in patients showing any defect of hepatic function or general debility.

Defective liver function, the result of the action of liver poisons, gives rise to definite symptoms which in an extreme form comprise the condition known as icterus gravis.

They are mental irritability, vomiting, twitchings of muscles, stupor developing into coma and often associated with Cheyne-Stokes breathing and convulsions. Death may occur within three days of the onset of these symptoms.

Jaundice, which may be slight or deep, is commonly, but not always, present. Hæmorrhages, e.g., hæmatemesis, melæna, hæmaturia or purpura may occur during the course of icterus gravis, and not uncommonly there is a marked rise of temperature immediately before death.

The condition of the liver found post mortem in cases of acute liver poisoning (icterus gravis) is one of acute yellow atrophy.

It is important to remember the dangers of damage to the liver in the therapeutic use of drugs having a toxic action on the liver. Thus, in giving arseno-benzol compounds at least a fortnight should be allowed between successive doses to enable the bulk of the arsenic to be excreted before the next dose follows, otherwise cumulative action may occur.

A characteristic feature of liver poisons is that the degeneration and destruction of the hepatic cells is usually followed by a replacement fibrosis. This fibrosis may become a chronic hepatitis and lead to a progressive

atrophic cirrhosis which produces characteristic symptoms years after exposure to the liver poison.

In October, 1927, there was under my care at St. Mary's Hospital a woman suffering from ascites and slight jaundice, the direct result of a cirrhosis of the liver, caused by tri-nitro-toluene poisoning contracted in a munition factory in 1916, at which time she suffered and recovered from an attack of toxic jaundice.

A fatal case of cirrhosis of the liver was brought to my notice in February, 1928. In this case the patient suffered from toxic jaundice due to tri-nitro-toluene poisoning contracted in a munition factory ten years previously. The liver was enlarged, hard and yellow. Microscopically it showed chronic inflammatory changes, with degeneration in the remaining liver cells.

These, and many other cases which I might quote, prove clearly that liver poisons not only produce an immediate damage to the liver tissue but that the harm does not stop there. It is often followed by a progressive hepatitis of a fibrotic nature. The same phenomenon is observed in the cirrhosis due to chronic alcoholism where the disease progresses steadily often when the consumption of alcohol has ceased.

Sometimes liver poisoning may result from a combination of poisons. I saw on March 12, 1928, a case of toxic jaundice in a patient who had on February 11 0.6 gm. salvarsan. On February 15 twelve septic teeth were removed under chloroform anaesthesia lasting over an hour. On March 9 a further dose of 0.6 gm. salvarsan was given intravenously.

In this case the liver poisoning was caused: (1) By the two doses of salvarsan; (2) by the chloroform anaesthesia; (3) by the septic absorption consequent on the invasion of the torn tissues from the dental extractions.

It cannot be too strongly insisted upon that great care is required in the therapeutic use of drugs which have a toxic action on

the liver. Overdosage and cumulative effect should be carefully avoided. It must be remembered that the damage caused is not a fixed quantity, but may be of a progressive nature leading to incurable and fatal disease.

PREVENTION OF LIVER POISONING.

It has been shown that liver cells stored with glycogen have an increased resistance to the action of toxic substances. It is therefore advisable before submitting a patient to the therapeutic action of a drug which has a toxic action on the liver to protect the organ three or four hours beforehand by a meal of glucose, 40 to 50 gm., which may be given with coffee and a little milk, also sweetened orange juice or other fruit juice may be given with advantage.

This procedure is advisable before intravenous injections of arseno-benzol, lead preparations, or other toxic drugs. It is also advisable before general anaesthesia with chloroform or ether.

NEW DRUGS.

At the present time there is a great tendency to use recently introduced drugs, many of which are of foreign manufacture, and are of synthetic organic nature.

These drugs are advertised extensively and their virtues greatly extolled. The advertisements rarely call attention to possible toxic effects, or dangers from their use. Dangers of addiction in the case of hypnotic drugs are rarely mentioned.

It is unfortunate that manufacturers of new drugs do not always take the medical profession fully into their confidence, and when introducing a new drug often fail to give adequate advice as regards care and caution in its use. The medical practitioner would have more confidence in the use of new drugs if he knew that all possible risks and dangers had been pointed out to him.

In May, 1927, in a paper read before the Royal Society of Medicine, I called attention to the numerous compounds of barbituric acid which are at present on the market

(veronal, dial, medinal, luminal, allonal, veramon, &c.). These drugs have a powerful therapeutic action, and in full and repeated doses may give rise to mental depression and serious nervous symptoms. Numerous cases of addiction have occurred from their use.

From 1905 to 1925, upwards of 257 cases of fatal poisoning in England and Wales have occurred from their use, and there appears to be no sign of diminution in these tragic occurrences.

Similar objections hold as regards the sulphonal group of drugs, and upwards of fifty-nine deaths have occurred during the same period.

Attention has been called to the quinoline group of drugs, atophan, atquinol, and atophanyl, which may have a serious toxic action on the liver.

It cannot be too strongly insisted upon that new drugs, especially those of organic nature and possessing hypnotic action, should be used with care and caution. Too frequent repetition of their use is to be avoided.

I should like to advocate a plea for the use of old and well-tried remedies of which the therapeutic action is thoroughly understood, and of which the value has been demonstrated by long experience.

Animal extracts are now largely used therapeutically, and it is well to remember the dangers from toxic effects. Thus, *insulin* is a substance of the utmost value when rightly used, but if given in an overdose may cause the characteristic and very dangerous symptoms associated with hypoglycæmia. In using it care should be taken to have available as antidote, if required, orange juice or glucose solution.

Pituitary extract must be used with care in cases of labour owing to its powerful action on the uterus and risk of rupture if given at too early a stage. It must also be used with care in cardiac weakness.

Adrenalin has a powerful physiological action and if given hypodermically must be

carefully used in small doses for fear of cardiac collapse.

Bacterial toxins in the form of vaccines or antigens require the greatest care in their use. There is a tendency at the present day to over-dosage. *Immunity* is a delicate bodily state and by judicious use of vaccine therapy may be increased with improvement in bodily health. *Overdosage* with vaccines may destroy immunity and impair the bodily health.

Animal sera usually of antitoxic nature are in common use. The possible danger of anaphylaxis should always be borne in mind. It can always be guarded against by the use of a preliminary small dose of 1 c.c. which if tolerated may be followed by the full therapeutic dose in an hour or two.

LEGAL ASPECTS.

There is no legal definition of the word "Poison." Its meaning, however, is sufficiently indicated by the phraseology of the legal sections relating to *criminal poisoning*. Thus, the expressions "poison or other destructive thing," "poison or other destructive or noxious thing," "to inflict upon such person grievous bodily harm," "any chloroform, laudanum or other stupefying or overpowering drug, matter, or thing," all relate to sections where the punishment for wilful intent in administering is felony.

In the section dealing with intent to injure, aggrieve or annoy any person, the expression "poison or other destructive or noxious thing" is used, and the punishment is "misdemeanour."

In the section dealing with abortion the term "poison or other noxious thing" is used.

The term "noxious thing" has been held to include all substances causing symptoms which might be dangerous to life or symptoms giving rise to pain, serious discomfort or incapacity.

In the case of abortion it includes all substances which might under the circumstances

in which they were administered reasonably give rise to any risk of abortion. In a recent case repeated doses of aloes in amount 2 gr. three times daily were held to be noxious. Quinine in doses of 10 gr. has been regarded as noxious. Oil of savin, tincture of cantharides, ergot, diachylon (lead plaster) have been held to be noxious.

The law regards poisoning with intent to injure or kill as a most serious crime and it is punishable by very severe sentences.

Death caused by poisoning even if the drug is administered lawfully and for a justifiable therapeutic effect is an unnatural death. Such cases must be reported to the coroner, who must hold an inquiry.

Examples are: Deaths immediately following an anæsthetic of any kind, or death directly due to the use of a drug for therapeutic purposes, e.g., arseno-benzol compounds, lead preparations, insulin, &c.

The holding of an inquiry by the coroner is an essential safeguard in the public interest.

In cases of death from accidental, suicidal, or homicidal poisoning, a coroner's inquiry is always held.

Homicidal poisoning has on many occasions given rise to great difficulty and anxiety to the medical practitioner in attendance on the case.

In such cases it is necessary for the medical practitioner to act with the greatest caution and tact, at the same time displaying a calm firmness. If he suspects that poison is being unlawfully administered to a patient under his care he should make sure that his suspicions are well grounded by insisting on analysis, by an experienced toxicologist, of the vomit (if any), urine, stools and any suspected articles of food or medicine to which poison may have been added. He should ensure that the patient is either removed to a nursing home, or if this is not possible, that reliable and skilled nurses have complete control over all that is administered to the patient in the shape of food or medicine.

The earliest opportunity should be taken for a consultation with another practitioner in whose judgment and experience he has complete confidence. It must then be decided on the merits of the particular case whether the legal authorities should be informed.

The Maybrick case was one of the most interesting examples of homicidal poisoning. Mr. Maybrick was ill, suffering from symptoms of gastritis, diarrhœa and neuritis. At first the symptoms were thought to be due to natural causes.

Dr. Humphreys, his medical practitioner, was called in on the third day of the illness. On the seventh day Dr. Carter was called in for consultation with Dr. Humphreys. Homicidal poisoning was suspected before death, which occurred on the eleventh day of the illness.

Arsenic was found in the Valentine's meat juice and milk, which were present in the bedroom. Mrs. Maybrick was found guilty of poisoning her husband with arsenic and was sentenced to death, though the sentence was commuted to penal servitude for life.

In many instances homicidal poisoning by arsenic has not been suspected by the medical man in attendance. This occurred in the *Seddon case*, where it was thought that the victim, Miss Barrow, had died from natural causes, and a death certificate was given. It was some weeks afterwards that suspicions were aroused and an exhumation was ordered by the Home Office. Analysis revealed the fact that death was due to acute arsenical poisoning.

In the *Armstrong case* the symptoms of Mrs. Armstrong, albuminuria, neuritis, vomiting, diarrhœa, &c., were put down to natural causes and a death certificate was given.

It was a year afterwards that suspicions were aroused as to the cause of death, and an exhumation was ordered by the Home Office. An analysis by the late Mr. Webster revealed the fact that the cause of death was acute arsenical poisoning.

In many cases the symptoms of poisoning so closely simulate natural disease that it is almost impossible to make a diagnosis on clinical grounds alone. Toxicological analysis is usually necessary before a definite diagnosis can be arrived at.

Veronal poisoning is a condition which has on some occasions been mistaken for natural disease. The presence of a high temperature and marked physical signs of broncho-pneumonia give the appearance of an ordinary toxic case of pneumonia. One of the symptoms of poisoning from a large dose of veronal is broncho-pneumonia. Analysis will show that veronal poisoning is the cause of the illness. This confirmation is readily obtained since veronal is excreted in large quantities in the urine, which should always be reserved for special investigation in a suspected case.

Sale of Poisons.—The numerous acts and regulations governing the sale of poisons in this country have served as a great protection to the public. In many noted trials the purchase of the poison by the accused person has been revealed by the record of the registers kept of the sale by the vendor.

This happened in the *Crippen trial*, where the purchase of hyoscine had been recorded in the Poison Register of the chemist.

In the Armstrong case the purchase of arsenic by the accused was definitely proved.

In the case *Rex v. Klosowski (alias Chapman)* 1903, the accused was proved to have poisoned three women with tartar emetic, and in the first two cases (afterwards exhumed) the certificate of death was given as being due to natural causes. At the trial the purchase of a large quantity of tartar emetic by the accused was proved by the production of the Poison Register.

The laws relating to the sale of poisons as at present framed, cannot keep pace with the rapid advances in chemistry and pharmacology. New therapeutic remedies and chemical substances of powerful toxic action are being discovered daily, and are not

comprised by the existing Schedules of Poisons.

If control is to be kept over the sale of poisons it seems that some comprehensive scheme must be devised which will include newly discovered substances of toxic action. This subject is one of great difficulty and is at present being considered by a special Departmental Committee.

DRUG ADDICTION.

This subject has of recent years become one of international action. The International Opium Convention of 1912 became ratified at the Peace Treaty of Versailles, and the consenting nations agreed to a joint course of action, and to the framing of Acts dealing with the "dangerous" drugs in question.

The meaning of "dangerous" in these Acts is not "dangerous to life," but dangerous as regards risk of causing "addiction."

The Dangerous Drugs Acts of 1920, 1921 and 1923, and the Regulations associated with them, are the result of this country participating in the International Opium Convention.

It is doubtful if drug addiction has ever been present to such an extent in this country as to call for the need of the Dangerous Drugs Acts. The Acts have undoubtedly been of great value, and since their enactment drug addiction has almost ceased as regards the development of fresh cases. It must be admitted, however, that the Acts have by their detailed regulations caused some inconvenience to medical practitioners, and have added to their work owing to the records required. On the pharmacist the burden of responsibility caused by these Acts and Regulations has been very much greater.

The dangerous drugs include opium, morphine, heroin, cocaine, and their preparations.

Amongst other drugs of addiction which endanger the public may be mentioned the barbituric acid group, the sulphonal group

and *cannabis indica*. It seems desirable that some control should be provided over the sale of these drugs similar to that given by the Dangerous Drugs Acts and Regulations. It does not appear necessary, however, that the same irksome regulations as regards the keeping of records, nor that the same heavy penalties should apply.

INDUSTRIAL POISONING.

This country may well be proud of the high position held as regards protection of its workers from risk of poisoning arising from their employment. The Home Office has done much to prevent risks, and by means of the existing Regulations under the Factory and Workshops Acts, and their efficient application, industrial poisoning has almost disappeared.

The names of Sir Thomas Legge and Sir Thomas Oliver will always be associated with the progress of industrial medicine in this country.

The notification of industrial diseases, due to lead, phosphorus, arsenical or mercurial poisoning, or anthrax infections, leads to prompt investigation, and preventive measures.

COMMERCIAL POISONING.

The great development in commercial and social life is associated with certain risks from poisoning which must be borne in mind. For example, the enormous use of petrol in motor vehicles and engines, &c., undoubtedly adds to the atmosphere poisonous gases of which carbon monoxide is the most dangerous.

This entails risk of poisoning and of impairment of health. Many cases of this nature have recently occurred.

Lead tetra ethyl has recently been introduced as an added constituent to commercial petrol. It is a substance which in the pure state is known to have powerful poisonous properties and may cause serious and permanent damage to the nervous system and other symptoms of lead poisoning. Since the onset of poisoning may be insidious

and much delayed the subject is one which requires careful investigation in the public interest. A special committee is being appointed to investigate this important matter.

An interesting example of commercial poisoning came to my notice a few months ago where *meta fuel*, the solid white substance which burns like spirit, was eaten by a boy of 16 in mistake for a sweet. From $\frac{1}{2}$ to 1 drachm was eaten. This caused in a few hours very serious symptoms of delirium, convulsions, coma and albuminuria. The patient made a good recovery but his life was seriously endangered.

The rapid and unceasing advances in science lead to the commercial and social use of newly discovered substances which may have an unsuspected poisonous action.

Scientific developments should be accompanied by unceasing watchfulness as regards possible toxicological dangers.

TREATMENT OF POISONING.

The cardinal principle in the treatment of poisoning should be removal of the unabsorbed poison without the least delay. If this were always remembered many lives would be saved. Where a poison has been taken by the mouth, unless it is a powerful corrosive, the stomach should be efficiently washed out as soon as possible so that any remaining poison may be completely removed from that organ.

Elimination should be promoted by free colon washing, and by the administration of aperients.

Where a poison has been injected subcutaneously free crucial incision and cupping will often enable some of the poison to be withdrawn and this will be facilitated by placing a ligature round the proximal portion of the limb if an injection has been made into that part of the body.

Suitable antidotes should be given *after* removal of the poison has been effected as completely as possible.

In the case of poisons producing prolonged coma, easily absorbable foods should be administered by the stomach tube at suitable intervals so as to maintain the strength of the patient.

Chemical poisons if absorbed in dangerous amount always produce serious damage to the bodily organs. When apparent recovery from the immediate symptoms has occurred, the "after-care" of the case is most important, thus complete rest in bed for several days so that such dangerous after-effects as syncope, &c., may be avoided.

ROUND THE WARDS.

A MAN of 57 was admitted to hospital with the following history: In 1913 he developed pulmonary tuberculosis in India and came home to an English sanatorium. There were then signs of infiltration in both lungs, and tubercle bacilli were found in the sputum in large quantities. After two years in a sanatorium the patient had lost his sputum, had gained 3 stone in weight and the disease was apparently arrested. He lived quietly in the country enjoying good health until the end of 1927. He then began to lose strength, cough and sputum returned, and he was found to be running a swinging temperature from 101° to 99° F. On examination, in addition to the signs of old fibrotic disease in both lungs, there was an area of dullness and weak breath sounds extending from the vertebral column to the posterior axillary line on the left side, and it was thought that he might have an abscess or localized empyema. The sputum was repeatedly examined, but as T.B. were never found it was considered most unlikely that the symptoms were due to a recrudescence of tuberculosis.

The dull area was shown by the X-ray as a dense shadow spreading out from the root into the middle of the left lung. On explora-

tion, the needle felt as if it was passing through some matter like cork, but no pus or fluid was found.

The possibility of neoplasm was considered, and as many cases have been recorded where carcinoma has been found in old tuberculous lungs, this was considered the most likely diagnosis. On the other hand, the patient had syphilis in 1898, and the Wassermann reaction was strongly positive. He was therefore given antisyphilitic treatment in the hope that the condition might be gummatous.

After three weeks' treatment, however, no improvement was noted, and although the treatment is still being continued it would appear that new growth is the most probable diagnosis.

EDITORIAL NOTES.

WE desire to call the attention of our readers to courses of post-graduate lectures in English which are to be held in Paris during the autumn.

These lectures will be given under the direction of the Paris University Medical School, and a certificate signed by the Professor and Dean of the Faculty will be given after each course to every doctor who has attended it regularly. The lectures take place in October and November, and include a course of ten, dealing with diseases of the bronchi.

Another course comprises nine lectures on diseases of the heart and vessels. The course on diseases of children consists of twenty-four lectures.

There are also courses on ophthalmology and diseases of the ear, nose and throat. One course deals with the surgery of the digestive tract, with operative demonstrations and operations on the dog.

Full particulars may be obtained from the Secretary, "Association pour le Déve-