powder, mixed with "ghee" (clarified butter) in their treatment of facial neuralgia and dogbite, or steeped in spirits as a lotion to promote the growth of the hair. They are said to administer the powdered root in cases of epilepsy and insanity.

The dried flowers of *datura alba* (called *Nai yeung fa*) can be bought in most Cantonese drug stores, where they are frequently dispensed for the relief of asthma and chronic dry cough, but the use of the seeds seems to be eschewed by the Chinese druggist.

TOXICOLOGY.

So far as is known at the present time the active principle of the *datura* plants is a mixture of a kind of atropine and hyoscyamine. The term "daturin" has been applied to this mixture, but the true nature of the component alkaloids has yet to be finally determined. Schmidt properly insists on speaking of stramonium atropine as contrasted with belladonna atropine; because, although chemically identical, some difference may be recognized both in their physiological and therapeutical actions.³

The medicinal dose of daturin has been given as $\frac{1}{2}$ mg. to 1 mg., or $\frac{1}{16}$ gr. to $\frac{1}{8}$ gr.,⁴ but it is difficult to say from the reports of fatal cases by *datura* poisoning how much daturin will constitute a fatal dose in any given case.

With regard to clinical experience of poisoning by the closely-related *datura stramonium* seeds, a child has died in twenty-four hours after swallowing a dose of 16 gr. (128 seeds), although 20 seeds had previously been dislodged by vomiting, and 80 by purging.⁵

Luff states that about 100 seeds form a fatal dose, death occurring in seven hours.⁶ Taking the mean of the proportions of the total alkaloid stated to be contained in the seeds by Squire⁷ and by Gunther⁸—namely, 0.5 per cent. and 0.318 per cent. respectively—this is equal to about $\frac{1}{25}$ grain of the alkaloid daturin. The whole plant is said to contain the active principle in the proportion of only $\frac{1}{50}$ per cent.¹⁰

Seventeen or eighteen gr. of the official extract of stramonium seeds (dose, $\frac{1}{4}$ to 1 gr.) have caused death.⁹ Recovery, on the other hand, has occurred after the vomiting of more than 100 seeds.⁹

RECENT CHEMICAL EXPERIMENTS.

Important points to discover are:

(a) The amount of poison which is present in the common *daturas* of the Federated Malay States.

(b) The relative degrees of strength of the poisonous principle in each.

(c) The difference, if any, between the daturin contained in *D. stramonium* and that contained in *D. fastuosa* and *D. alba*. I have attempted to elucidate this by examining both the fresh plants and the dried seeds. The experiments were made at the Institute for Medical Research at Kuala Lumpur. I am greatly indebted to Dr. H. E. Durham for the results that have so far been obtained by them, and have much pleasure in expressing my appreciation of the valuable experience which his kindly instruction has afforded me. It was found that the mixed alkaloids could be easily removed from an ammoniated extract by shaking out with benzol. In the case of a full-grown *datura alba* plant which was treated in this way, the refuse remaining after extraction by benzol was found to have no further mydriatic effect on a cat's eye, and had no poisonous effect when given in large doses to a puppy. It was therefore concluded that the whole of the active principle had been removed by means of the benzol. Want of time and opportunity prevent me from making further experiments in this direction, but I hope to resume my investigations on account of the great importance of this branch of the subject.

DATURA POISONING; TREATMENT.

Cases of poisoning by *datura* are generally treated by more or less time-honoured methods. It has been proved, however, that implicit reliance cannot be placed on emetics, and the early administration of a purgative is often advisable. Daturin is precipitated by tannic acid; and the use of any decoction containing tannin, such as tea or coffee, which is strong enough to destroy the active principle, may be of value. Like atropine, it is excreted from the system by means of the kidneys.

Opium administered by the mouth or through the rectum, the various salts of morphine, pilocarpin, and chloroform inhalations have been given successfully in cases of stramonium poisoning, but no chemical antidote by which daturin has been decomposed in the animal economy ap-

pears to have been either used or suggested up to the present time.

Nevertheless, there is reason to believe that we possess an efficient antidote in potassium permanganate. Potassium permanganate has the important chemical property of oxidizing the vegetable alkaloids, and has been used with success in many cases of opium poisoning. This salt may be introduced into the stomach without danger in solutions not stronger than 1 gr. to the oz. Washing out, therefore, by means of a tube with a dilute solution of this strength appears to be indicated so long as any *datura* remains in the stomach.

Experience alone can settle the question as to whether the potassium permanganate will be of any therapeutic use after daturin has been absorbed into the system, but as the action of the poison is doubtless prolonged, especially when taken with large quantities of food, we should expect that repeated small doses would be of great value in many cases.

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EXPERIMENTAL HAEMOGLOBINURIA IN A CASE OF BLACKWATER FEVER.

UNDER THE CARE OF

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REPORTED BY

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INABILITY to take quinine is a bar to residence in highly malarious countries. Therefore, idiosyncrasy in the direction of quinine haemoglobinuria is a definite indication against return to West Africa. When the patient (who is the subject of the following notes) declared that quinine always gave him black water, and we were requested to advise his employer as to his future for further service in West Africa, and as he expressed willingness to give a demonstration of the fact, his offer was accepted partly in his own and his employer's interests, and as an object lesson for the students at the London School of Tropical Medicine.

T. R., aged 25, English, last from the Gold Coast Colony, was admitted on March 10th, 1903.

Previous History.—He went to the Gold Coast in June, 1901, and had his first attack of fever in January, 1902; it was not severe, and he was not laid up. He had three similar attacks up to September, 1902, and was always treated with quinine, 10 gr. at a time, and also took this dose irregularly at considerable intervals as a prophylactic. In October, 1902, he had an attack of blackwater fever; the first symptoms led him to believe that he was about to have an attack of malaria. He took 10 gr. of quinine at 5 p.m. one evening (he cannot remember the date), and about midnight he had vomiting, diarrhoea, and frequent micturition. He noticed that his urine was black. He was attended by a doctor, who stated that his temperature at one time was 107°. He was in bed three days and was deeply jaundiced. The black water passed off in twenty-four hours, and he had no further attack in Africa, and arrived home early in March. On March 11th, feeling chilly and feverish, he took 10 gr. of quinine at 7 p.m., and at midnight diarrhoea and vomiting set in, and he began to pass black water. All symptoms had disappeared in the morning. He consulted Dr. Manson, who sent him for observation and experiment to the Branch Seamen's Hospital in connexion with the London School of Tropical Medicine.

State on Admission.—On March 10th, 1903, temperature 99.6°; isanaemic, spleen enlarged, not tender.

Blood Examination.—No malarial parasites; no pigmented leucocytes. Red corpuscles, 3,425,000; leucocytes, 10,000; haemoglobin (von Fleischl), 65 per cent.

Differential Leucocyte Count.—Polymorphonuclear, 59 per cent.; large mononuclear, 18 per cent.; lymphocytes, 21 per cent.; eosinophiles, 1 per cent.; mast cells, 1 per cent.

On the following day the temperature was normal and he felt quite well—he remained so until March 23rd, when Dr. Manson decided to test his statement that quinine gave him haemoglobinuria. His blood was examined during the day and gave red corpuscles, 3,635,000; leucocytes,

7,000; haemoglobin, 65 per cent. At 9 p.m. he was given the 10 gr. quinine by the mouth. He slept until 1 a.m., when he had a moderate rigor, nausea, and diarrhoea, and passed a large quantity of black water. His temperature was 99° at 2 a.m. In the morning his urine began to clear, and by 7 p.m. was pale yellow, his temperature then being 98.8°. The examination of the black sample of urine showed one-third albumen, methaemoglobin crystals, and a few haemoglobin casts; the spectroscopic also showed methaemoglobin.

Blood Examination, 11 a.m.—Red corpuscles, 3,000,000; leucocytes, 10,000; haemoglobin, 59 per cent.

Differential Leucocyte Count.—Polymorphonuclear, 77 per cent.; large mononuclear, 8 per cent.; lymphocytes, 13 per cent.; eosinophiles, 1 per cent.; mast cells, 1 per cent.

This examination showed a loss of over half a million of red corpuscles in a few hours.

On March 25th his anaemia was marked and he was slightly jaundiced.

Blood Count.—Red corpuscles, 3,000,000; leucocytes, 11,800; haemoglobin, 57 per cent.

Differential Count of Leucocytes.—Polymorphonuclear, 56 per cent.; large mononuclear, 21 per cent.; lymphocytes, 20 per cent.; eosinophiles, 2 per cent.; transitional, 1 per cent.

On March 26th daily hypodermics of 15 minims of Squire's arsenate of iron were ordered, and on the 27th euquinine gr. 2 three times daily. His progress was favourable, but his blood regeneration was slow.

Blood Count (March 30th): Red corpuscles, 3,320,000; leucocytes, 6,200; haemoglobin, 58 per cent.

He left on March 31st with instructions to continue iron and arsenic and euquinine for one month.

This experiment, deliberately planned and carried out, is one more proof that in some individuals under certain unknown conditions quinine produces haemoglobinuria. The antecedents of the case seem to indicate that the conditions which led to the formation (so to speak) of the haemoglobinuria idiosyncrasy were brought about by neglect of the use of quinine in the earlier stages of what may have been a special form of malarial infection and the consequent development of an intense and peculiar cachexia.

HODGKIN'S DISEASE AND ARSENICAL POISONING.

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THE following case of Hodgkin's disease is of particular interest from the effect of arsenic given medicinally.

A lady, aged 58, noticed in June, 1901, some slight swellings in the neck; she also for a few months before had been getting short of breath on slight exertion. In July she consulted a physician in London, who found "enlarged glands, occipital, cervical, subclavicular, inguinal, abdominal and pelvic, varying in size from a pea to a chestnut, all quite distinct, rather firm and hard." She also had slight oedema of the feet. In the lungs there were some scattered rhonchi, and the air entry in the lower half of the left lung was deficient, presumably from pressure of mediastinal glands. He diagnosed Hodgkin's disease, and ordered liq. arsenicalis *mv ter die*. At the end of a fortnight she went to him again feeling very much better, less short of breath, with no oedema of the feet, and a distinct diminution in the size of the glands, but she complained of a burning pain in the soles of her feet and had a slight purpuric rash on her shins. In consequence the arsenic was stopped, but there came on keratosis of the soles and slightly of the hands, followed by desquamation, increased pigmentation of the skin, and four weeks after the stopping of the arsenic a severe attack of herpes of the right side of the neck. This was succeeded by most intense and persistent neuralgia, which resisted all treatment. During this time the glands all rapidly decreased in size and in two and a-half months had almost disappeared, but then began to enlarge again.

When she came to Brighton at the beginning of October, 1901, she still had intense neuralgia and hyperaesthesia of the right side of the neck, but otherwise was in fair health. A few glands could be felt in both sides of the neck and in the groins, but none were larger than small beans. There was no evidence of mediastinal pressure, the heart and lungs were normal, and neither liver nor spleen were enlarged. The blood showed no leucocytosis. Under phosphorus there seemed no increase of the glands for three weeks, but they then began to enlarge rapidly. I then tried liq. arsenicalis in 2-minim doses, but in ten days there was some tingling in the feet and pain in the calves of the legs, so a return was made to phosphorus in large doses, and also as disinfectants of the alimentary tract sodium sulphocarbolate and perchloride of mercury; I regret that a trial was not given to lavage of the stomach, which has proved so beneficial in a few cases, but there was no evidence of dilatation. The glands steadily increased in size, the liver could be felt below the costal margin and the spleen was also enlarged. She had an irritating cough and was short of breath, the air entry in the left lower lobe was diminished. Since nothing delayed the disease except arsenic, I determined to try sodium cacodylate, and, beginning with $\frac{1}{4}$ gr. hypodermically, I increased up to $\frac{1}{2}$ gr. at the end of the week; after a week's interval without injections there was a slight diminution in the size of the glands and no symptoms of arsenical poisoning; $\frac{1}{2}$ gr. was then injected every day for another week and the improvement continued. After

another interval of a week $\frac{1}{2}$ gr. was injected every day for a third week. At the end of this there was a trace of albumen in the urine, so I deemed it safer not to give any more cacodylate.

The glands slowly decreased and all went well till the fifteenth day, when an acute attack of pleurisy started on the left side; she also complained of pain in the legs, which were slightly swollen. Two days later there was a friction rub on the right side and evidence of a moderate amount of fluid in the left chest; the legs were very oedematous and painful with several deep red erythematous patches upon them. Her pulse was 120, temperature not higher than 99° at night; the urine contained no albumen. Fluid rapidly accumulated in the right chest but did not increase in the left, there was also some fluid in the abdomen. A fortnight after the onset of the pleurisy I drew off 28 oz. of grey milky fluid from the right chest, a week later 32 oz. of the same fluid not quite so milky, and by Southey's tubes 15 oz. of serum from the feet. A fortnight later a final aspiration drew off 36 oz. of quite clear fluid from the right chest. The milky fluid did not look like pus, though microscopically it contained large numbers of leucocytes. The glands all rapidly diminished in size meanwhile, and the oedema of the legs quite disappeared and she seemed to be making progress for a time, but the swelling of the glands began to return, and she finally developed great irritability of the stomach, which resulted in her death from exhaustion in April.

This is a case of Hodgkin's disease in a person peculiarly susceptible to arsenic; it is interesting to note that the glands diminished under arsenic with quite unusual rapidity. The pleural effusion, ascites, and oedema I cannot help attributing to the sodium cacodylate, since the glands were steadily becoming smaller before and during this part of the illness, and these symptoms were present in some of the victims of the recent arsenical beer epidemic.

In going through the literature of Hodgkin's disease, a case reported by Dr. J. H. Bryant in the BRITISH MEDICAL JOURNAL of September 14th, 1901, p. 706, struck me as of peculiar interest.

A man, who had noticed the presence of enlarged glands for four years and had been unable to work for the past six weeks, and presumably had been under treatment outside, was admitted to hospital with the gland trouble well marked, but in addition he had a cough and occasionally spat up bright red blood. No tubercle bacilli could be found and there was no evidence of phthisis; he had a right pleural effusion. He used to "vomit after meals, and also complained of an acid taste in his mouth"; another troublesome symptom had been "itching of the skin, which was rather dusky." There was some albumen in his urine; the pulse was 108. He was ordered 6 minims of liq. arsenicalis three times a day. A fortnight later "there was marked oedema of both legs, the penis and scrotum, and over the sacrum and abdomen up to the manubrium." A fortnight later still the skin appeared to be more dusky, the dullness had increased on the right side of the chest to the level of the second rib. The arsenic was increased to 7 minims. A week later paracentesis abdominis drew off "5½ pints of turbid and rather milky fluid. The turbidity was not cleared up by ether; a good many leucocytes were found, but no fat globules." A week later "9 pints of chylous fluid were withdrawn"; a week later still 63 oz. of clear fluid were drawn from the right chest, and the abdomen was again tapped. Then the man died.

Turning to Dr. E. S. Reynolds's description of arsenical poisoning in the BRITISH MEDICAL JOURNAL of December, 1900, one finds: "The face is dusky red.....In many cases there is persistent vomiting.....In some cases much itching of the skin.....A few patients have spat blood, there being no symptoms nor physical signs of phthisis.....There is sometimes very marked general oedema like that seen in beri-beri."

One can hardly doubt that the case I have just quoted suffered from arsenical poisoning. Then, as to the fluid drawn off from the abdomen, it is called chylous, evidently because the cause was supposed to be blocking of the lacteals by large glands; but the description "turbidity, not cleared up by ether, a good many leucocytes but no fat globules," shows that it is not chylous, but of the same nature as the fluid drawn from the pleural cavity in my case.

At the necropsy "three pints of yellow fluid were found in the right pleural cavity. The right lower lobe was covered with recent yellow lymph which readily peeled off, beneath it were many subpleural ecchymoses. Several hard nodules could be felt in the lower lobe of both lungs. There was a good deal of fibrous tissue infiltrating the lungs. Microscopically the nodules were made up chiefly of fibrous tissue, and in places there were collections of lymphoid cells." After the description of the other organs there came the following remarks: "The macroscopic appearances of the organs were most peculiar and by no means characteristic of lymphadenoma. The most marked feature presented by the sections examined microscopically was the large amount of fibrous tissue present. This was peculiarly noticeable in the glands, spleen, and liver. In the liver the fibrous tissue was unequally grouped between the nodules, but was by no means confined to this area, for in many places it was infiltrating the lobules themselves, here and there replacing and here and there surrounding the liver cells; in fact, the change had the appearance of a mixed interlobular and intracellular cirrhosis. There was only one part of the body in which a lesion quite typical of lymphadenoma could