disappeared during the day. The rash differed from the usual urticarial eruptions being very slightly raised above the surface of the skin. The itching led to sleepless nights followed by languor and weakness during the day. There were vague pains in the abdomen, signs of indigestion and toxic headaches. Appendicitis was suspected and the appendix duly removed without any relief of symptoms. Various prescriptions were tried internally and externally for the skin condition unsuccessfully. There was a history of having passed blood and mucus before the onset of the trouble. On plating out *B. para-dysentericus* (Castellani) was isolated from which a vaccine was prepared and administered. The condition has not returned for about 18 months.

Case 2.—S., a girl of 18 years, came to Maymyo for change of climate. Every evening she got a temperature of 99—100°F.

There was tenderness in the abdominal region and sometimes diarrhœic motions were passed. She had lost weight and her condition had been diagnosed as tabes mesenterica. *Streptococcus hæmolyticus* (*see* table above) was isolated and an autogenous vaccine prepared. Since the administration of the vaccine (9 months interval) her health has given her no trouble and she has been able to pursue her studies successfully.

Case 3.—B., a retired engineer, 75 years of age, was suffering from diarrhœa off and on for years. There was anorexia, indigestion and gradual loss of weight. From the stools *Streptococcus equinus* was isolated and an autogenous vaccine administered. The condition improved miraculously, the weight increased and the diarrhœa stopped. The case was followed for two years but his 'sprue condition' as he called it did not return.

Case 4.—X., an old man aged about 55 years, rather obese, developed an evening temperature usually rising to 101°F. At the time of examination of the stools he was losing weight, suffering from diarrhœa and complaining of pain in the hepatic region. He had passed mucus in his stools years ago and his habits had been intemperate for the last 20 years. *Streptococcus fæcalis* was isolated from the stools and an autogenous vaccine duly administered. His abnormal temperature never returned (during 8 months) though off and on he got diarrhœa and 'liver'. He gained in weight, developed a good appetite, and the occasional diarrhœa did not seem to bother him as he was aware that it was due to indiscretions in liquid and solid nourishment.

Another case which requires special mention, being of clinical importance, is that of a retired extra-assistant commissioner who came to one of us suffering from 'piles'. He stated that about five months previously he had attended a marriage feast, which he fully enjoyed and ascribed constant bleeding to that particular occasion. He tried several treatments, local astringent applications as well as internal remedies for the 'hæmorrhoids'. No mass was projecting externally but the stools with blood and mucus showed vegetative forms of *Entamœba histolytica* in large numbers. Administration of emetine stopped the bleeding 'miraculously' as the gentleman described it.

One case showed vegetative forms of *Giardia* and another had *E. histolytica* cysts during the acute stage.

Post-dysenteric infections

This is a record of study of 13 patients, who though they had got over the acute stage of dysentery were still having some clinical symptoms referring to the gastro-intestinal tract. Almost all of them were chronic cases, giving a history of old dysentery and were having flatulence, diarrhœa, 'acidity' in the stomach, indigestion, tenderness in some part of the abdominal region together with certain other toxæmic symptoms.

The technique followed was similar to the one described above, the stools being plated out on litmus-lactose-bile-salt agar media. With a magnifying lens the streptococcal looking colonies were found in large numbers in all except two cases. As it was a different picture from the normal, vaccine treatment was tried in these cases with decided benefit. Much stress has not been paid to this point as it was not possible to follow up all the cases but those recorded in Table I are interesting.

The exceptions referred to above were *Staphylococcus citreus* and *B. para-dysentericus* (Castellani). Table I shows the biochemical reactions of the organisms isolated.

A PRELIMINARY NOTE ON THE ABSORPTION OF 'MAKARADHWAJA' (SULPHIDE OF MERCURY)

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Indigenous Drug Series No. 37

'MAKARADHWAJA' is a well known inorganic preparation of the Hindu Pharmacopœia. Its use can be traced to the time of Bhabamisra, the renowned Hindu physician, who lived in the early part of the 16th century. Since then, the preparation has been in constant use and is to this day held in very high esteem by the Ayurvedic practitioners. This drug has such a great hold on the minds of the people in India that many practitioners of Western medicine also use it. There is probably something of real value about it, as it has resisted the ravages of time for many centuries and is universally esteemed to the present day.

Preparation of 'makaradhwaja'.—It is necessary at the outset to outline the process of preparation of this drug, as according to the Ayurvedic Pharmacopœia a great deal depends on the method adopted. Various methods of preparing the drug have been described in books on Hindu medicine. The description given below has been kindly given to us by an eminent practitioner of Ayurvedic medicine in Calcutta and is believed to be the standard method laid down in books of the Hindu materia medica.

Eight parts of pure mercury and one part of gold-leaf are mixed together to form an amalgam. To this mixture, sixteen parts of sublimed sulphur are added and the resulting mixture is rubbed very thoroughly in a stone mortar with a stone pestle for 24 hours or more

until the whole is converted into a lustreless, fine impalpable powder of uniform consistence. This powder should be light enough to float on water and there should be absolutely no lumps or grit in it when rubbed between the fingers. This is known as 'kajjali' in Sanskrit and its chemical composition is said to be the same as black sulphide of mercury. This preparation forms the basis for the 'makaradhwaja'. The 'kajjali' is placed in a narrow-mouthed bottle and is gradually heated on a sand bath. When the temperature reaches a certain limit the bottle is filled with reddish fumes of various hues. On cooling 'makaradhwaja' is found deposited on the inner surface of the bottle. The sublimed powder is collected by breaking the neck of the bottle and scraping off the deposit, which is then preserved in a clean dry vessel for future use.

A great deal of stress has been laid by the Hindu physicians on the purification of the mercury employed for the preparation of this drug. The mercury used has to be passed through various methods of purification laid down in the Ayurvedic books, before it can be accepted for use. These processes are known as 'sodhana' or correction of the metal. It may be mentioned in this connection that the processes described for 'sodhana' are very tedious and complicated. Judged from the standpoint of modern chemistry, these methods of purification have very little to recommend them, and in many instances impurities from extraneous sources are actually introduced in the different stages of the processes, rather than removed.

Administration of 'makaradhwaja' in Hindu medicine.—'Makaradhwaja' is seldom used alone. In the majority of cases, it is mixed with various drugs called 'anupana' or adjuvants. Thus in cases of indigestion and diarrhœa, 'makaradhwaja' is mixed with powdered 'bael' fruit (*Ægle marmelos*); in cases of fever and cough it is given with the juice of ginger, betel leaves (*Piper betle*) and tulsi leaves (*Ocimum viride*); in heart disease it is combined with musk. In the absence of proper 'anupana' (adjuvant), honey may be used in every case. The usual procedure is to take a dose (approximately one grain) of 'makaradhwaja' with 60 drops of the 'anupana' or honey and rub it for some time in a stone mortar before administration. The medicine may be used both for adults and children, the dosage being regulated according to age. 'Makaradhwaja' when taken regularly is believed in the indigenous system of medicine to be a wonderful tonic, and is said to increase the longevity of the patient.

The composition of 'makaradhwaja'.—Chemically, 'makaradhwaja' is identical with the red sulphide of mercury. This sulphide occurs in nature as the mineral ore called cinnabar in many parts of the world, particularly in California, China and Spain. In the vernacular, Cinnabar is known as 'hingool' and is to be found in Nepal. 'Hingool' found in the Calcutta market is not the natural ore, but is artificially prepared by heating mercury with sulphur in a retort. This substance, except for the slight impurities which it might contain, has the same composition as 'makaradhwaja'. In Ayurvedic practice, however, 'hingool' and 'makaradhwaja' are claimed to possess entirely different properties. Not only is the latter considered different from 'hingool' (the natural red sulphide of mercury), but it is also thought to be different from the artificial sulphides of mercury like 'kajjali' and 'krishna-parpati' (both of which resemble black sulphide of mercury in composition) and 'rasa-sindura' (red sulphide of mercury). These differences are rather difficult to explain from the modern scientific point of view. It is claimed by the Ayurvedic practitioners that 'makaradhwaja' is not ordinary red sulphide of mercury but is a combination of sulphide of mercury with gold. This conception however has not received any support from the investigations carried out by Dr. Neogi of the Presidency College, Bengal (1910-11). He has shown conclusively that gold does not enter into combination with mercury compounds used in the indigenous medicine like 'makaradhwaja', 'rasa-sindura', etc.

Pharmacological action.—Most of the soluble salts of mercury are readily absorbed from the intact mucous membrane of the alimentary tract. They are said to be acted on by the acid, alkali and proteins present in the gut, are converted into oxides and later into albuminates, in which form probably they enter the blood. There is, however, a great deal of difference in the rate of absorption of the different insoluble mercury salts. Mercurous chloride and mercurous iodide are known to be very slowly absorbed, as mercury has been definitely detected in the urine after their administration. It has been found that after administration of 0.6 gm. of calomel and 20 mgm. of mercurous iodide daily, 5 mgm. and 4 mgm. of mercury respectively are excreted in the urine. In the case of the sulphides a great deal of doubt exists as to whether they are absorbed at all. The sulphide ion is very inert and it is clear that unless and until the salt is dissociated into its constituent ions, mercury will not be able to exert its influence on the body tissues. Sulphide of mercury is not used in any of the pharmacopœias of Western countries as it is considered to be devoid of therapeutic activity. This idea gains additional support from the fact that the various mercurial salts after absorption are excreted into the cæcum and colon as sulphides, and in this form also mercury is found in the fæces. In the Ayurvedic Pharmacopœia, on the other hand,

mercury is predominantly used in the form of sulphides. It is indeed strange that a country where this metal was first harnessed into the service of medicine, should have chosen an insoluble and possibly an inert salt for therapeutic uses. We therefore thought it worth while to investigate whether this salt is rendered at all soluble under ordinary physiological conditions in the gut, and whether the mercury ion liberated from this so-called inert combination can be utilised by the tissues.

Experimental.—Ghosh (1931) has recently shown that the sulphides of mercury in a fine state of division undergo solution in 5 c.cm. of a 0.3 per cent. solution of HCl at 100°F. in an hour. This is also true when these sulphides are digested with filtered gastric juice obtained artificially from a healthy patient. If sulphide of mercury is broken up in this manner by the acid of the gastric juice, it is likely that absorption will take place. By feeding a young dog with finely powdered 'makaradhwaja' once a day for three consecutive days, he has further shown the presence of mercury in the liver. From these observations, he concludes that the insoluble sulphides are changed into soluble chlorides by the action of the gastric juice and in this form mercury is absorbed into the system *via* the portal circulation and stored up in the liver and other organs. This observation is based on only one animal experiment and cannot therefore be considered to be a definite proof of the absorption of the metal. In order to confirm the findings, we studied the absorption of the drug from the stomach and intestines by the following methods. The abdominal cavity of guinea-pigs was opened under ether anæsthesia in the epigastric or iliac regions as required, and sterilised catgut ligatures were placed at the pylorus in three animals and at the ileo-cæcal junction in two others. A window was made into the wall of the stomach and finely powdered 'makaradhwaja' suspended in honey was introduced directly into the cavity, through the wound. The wounds in the stomach and abdomen were sutured and the animals allowed to recover from the anæsthesia. After this operation, the animals generally died within 24 to 30 hours. *Post-mortem*, the small intestines and the colon were ligated separately and their contents examined for the presence of mercury. Under ordinary circumstances, if the insoluble sulphide of mercury is converted into the soluble chloride and is absorbed into the system as suggested by Dr. Ghosh, we would get some evidence of the presence of mercury either in the liver, where it would have been stored, or in the colon washings, where it would have been excreted. As nothing has been allowed to pass through the pylorus in the first series of three animals and through the ileo-cæcal valve in the other two, the presence of mercury in the colon would be a fairly reliable indication of its absorption and circulation in the blood. In all the guinea-pigs where 'makaradhwaja' was introduced into the stomach in the manner described above, we could not detect the metal in any of the washings from the intestinal tract, neither was there any definite indication of its storage in the liver, at least in sufficient amounts to be distinguishable by the ordinary chemical tests for mercury. From these experiments, it may be said that mercury in the form of 'makaradhwaja' is not absorbed either from the stomach or the small intestines. It is, however, likely that very minute quantities are absorbed and excreted, and the ordinary chemical tests are not sensitive enough to detect its presence. Further investigations with improved methods of identification of mercury are therefore called for.

Excretion of the drug was next studied as the rate of elimination is a very good index of the rate of absorption and presence of a drug in the blood and tissues. 'Makaradhwaja' was obtained from reliable sources as most of the preparations in the market are said to be adulterated. It was administered to several healthy patients in doses of 1 to 2 grains (65 to 130 mgm.), following strictly the directions of the Ayurvedic practitioners. The drug was thoroughly rubbed in a stone mortar for about 15 minutes before administration to convert it into a fine, impalpable glossy powder and was mixed with pure honey as a vehicle. It was given daily for one week. After the first three days, samples of the urine were collected daily and examined according to the methods to be described later. Individual samples as well as samples from 24-hour collections (kept with toluene to prevent decomposition) were examined. Most of the volunteers were our laboratory assistants who were healthy young men and were under strict control.

In such a study, the excretion of the metal in both the urine and fæces has to be considered. Most of the analytical methods of estimation of the metal in vogue contain inherent faults, and any conclusions drawn as a result of estimation by these methods are likely to be fallacious. Booth, Schreiber and Zurick (1926) have described a new analytical method which has been claimed to yield accurate results and permits of the estimation of 5 mgm. or less of mercury in a litre of the solution in presence of organic matter. In principle, it consists of the oxidation of the excreta by digestion with sulphuric acid and potassium permanganate, precipitation of the mercury as sulphide and enmeshment of the precipitate by gelatinous manganic hydroxide. The washed and dried precipitate is ground up with lead chromate and decomposed by heating in a glass tube at 550°C. for 3 hours. The volatilized metallic mercury is condensed in the cooled portion of the tube. When the entire mercury has been separated, it is collected into one globule,

transferred to a calibrated capillary tube, the length of the column measured micrometrically and transposed to the corresponding weight. As this method entails the selection of cases who have to be kept under strict hospital supervision for the purpose of collection of the daily excreta for weeks, we tried to estimate the mercury excreted in the urine as a preliminary measure. The following method which is a slight modification of the original Bardach method was used:

To 250 c.cm. of well shaken unfiltered urine, 5 gms. of aluminium sulphate and ammonia were added. The mixture was then heated and filtered while hot. The precipitate was washed with hot water and dissolved in concentrated HCl. A bright clear copper foil was introduced into the solution which was set upon a water bath for 45 minutes. The amalgamated copper foil was removed, washed with distilled water and then with alcohol and finally with ether and dried in the air. A minute particle of iodine was introduced into a test tube and the copper roll was put in and gently heated. A yellowish or reddish deposit indicates mercury. This test is quite sensitive and allows the detection of as little as 0.01 mg. of mercury in a solution.

In seven healthy individuals experimented upon no traces of mercury could be detected in the urine by this method. The stools in some of these cases are being examined but the results are not yet conclusive. Further observations on these lines are being conducted with administration of 'makaradhwaja' for 2, 3 and 4 weeks and the results will be reported in due course.

Therapeutic uses.—'Makaradhwaja' is commonly used as a tonic in debilitating conditions and in convalescent patients after acute illness. In failing circulation and in cardiac asthenia, 'makaradhwaja' is considered to be a sovereign remedy.

Recent work has shown that the mercury ion in a high state of dilution has a definite stimulant action on animal tissues. A 1 in 1,000,000 strength of mercuric chloride added to the perfusate distinctly stimulated the isolated mammalian heart and increased its force of contraction. It is therefore likely that if absorption does take place in very small quantities, 'makaradhwaja' might produce a stimulant action on the heart. In view of this work, the senior author tried this drug in a few myocardial disorders following acute specific fevers. That there was distinct clinical improvement in the condition of individual patients after the administration of the drug for a period of 15 to 20 days there seemed little doubt, but extended trials are necessary before a definite opinion can be given. Mercury preparations have been used for many years as tonics and alteratives in Western medicine. There seems to be very good reason for such uses as it has been shown that small doses of mercury diminish the amount of oxidation of the tissues, as evidenced by the variations in the gaseous interchange. Further, the administration of small doses of mercury to rabbits, dogs and men causes an increase in the number of red blood corpuscles, while the body gains in weight and the general nutrition is improved. Larger doses, however, have been found to act in the reverse way by causing a diminution in the amount of hæmoglobin, and the number of corpuscles, and in the weight. Most of the preparations of mercury in use in the British Pharmacopœia are rapidly absorbed, so that larger quantities of mercury ion than are good for the system are probably taken up. It is quite possible that in 'makaradhwaja' we have an insoluble preparation, which by action of the gastro-intestinal juices is rendered absorbable to such an extent that minute quantities of mercury ions sufficient for stimulation of the tissues and no more, are taken into the system and are acting on the tissues.

'Makaradhwaja' is also used as a laxative with good results, particularly in those cases when there is visceroptosis and an atonic condition of the gastro-intestinal tract. As an intestinal antiseptic also, it is said to be of great utility and is supposed to relieve the gaseous distension of the bowels due to fermentation. How far this is true has yet to be investigated, but mercury is known to be a powerful and readily diffusible protoplasmic poison, which acts in very high dilutions against lower forms of life. Recent researches on the intestinal antiseptics have shown that calomel is one of the few drugs which produces alteration in the intestinal flora and brings about an appreciable decrease in the bacterial contents of the gut. In view of these facts it is not unlikely that the claims made for 'makaradhwaja' in this connection may be borne out by further research.

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RABIES IN THE MONGOOSE

(REPORTS FROM RECORDS, INCLUDING A REPORT ON THE FIRST POSITIVE BRAIN OF MONGOOSE EXAMINED AT KASAULI. COMMENTS INCLUDING SPECULATION AND BEARING ON TREATMENT.)

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I. Reports from records including a report on the first positive brain of mongoose examined at Kasauli.

1. *Case No.* 2877 *of* 1932

H. S., aged 60, male, of K. K., district Ludhiana. Bitten on 29th April, 1932. Came for treatment on 1st May, 1932. Finished treatment on 14th May, 1932. He stated:—

'I was watering my oxen in the animal shed when a mongoose rushed in amongst them. I lifted it up and