On the Action of Senecio Alkaloids and the Causation of Hepatic Cirrhosis in Cattle. (Preliminary Note.)

By Arthur R. Cushny, F.R.S.

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(From the Pharmacological Laboratory, University College, London.)

The various species of Senecio in this country are generally regarded as harmless, the chief of them being the common ragwort and the common groundsel. In Nova Scotia, New Zealand, and South Africa they have, however, been associated with hepatic cirrhosis in cattle, which is known as Pictou, Winton, and Molteno disease in these countries. The species which induces this condition in Canada and New Zealand is apparently identical botanically with the common ragwort of this country, *Senecio Jacobœa*, while in South Africa the Molteno disease is associated with the *Senecio Burchellii* and the *Senecio latifolius*.

The symptoms of the disease are practically identical in these localities. The cattle are observed to be badly nourished for some time, but definite symptoms appear only three or four days before death, commencing in diarrhœa, dry and staring coat, and disinclination to feed. The cattle then lie down, or sometimes become frenzied and charge anyone who approaches. Soon coma and unconsciousness set in, and death follows.

The liver is found to present the appearance of chronic cirrhosis in some cases, in others there is marked venous congestion of this organ. The gall-bladder is distended with viscous, generally dark-coloured, bile, and there may be petechiæ in this organ, in the urinary bladder, and heart. The fourth stomach contains hæmorrhages and sub-mucous exudations. The intestine is inflamed around the openings of the bile ducts.

The disease being of great economic importance, a number of investigations have been instituted, which have proved that it is due to feeding on these species of Senecio.

With regard to the chemistry of the Senecio genus, Grandval and Sejour found two alkaloids in the common groundsel, which they term senecionine and senecine, and Watt found two others in the *Senecio latifolius* of Cape Colony, and has named them senecifoline and senecifolidine. These two bases were sent to me for pharmacological examination by Prof. W. R. Dunstan, and I have done a number of experiments with them, chiefly upon cats.

The symptoms induced are of two kinds, acute and sub-acute. The acute symptoms commence with nausea and salivation, extremely accelerated respiration, and, somewhat later, violent clonic convulsions under large doses. These acute symptoms generally pass off in the course of two or three hours, and the animal appears perfectly well very often for the next two or three days or longer. Some loss of weight may occur during this time, and then the sub-acute symptoms are introduced by a stool of rather loose consistency, loss of appetite, and in some cases vomiting. The animal then becomes weak and disinclined to move, and passes into a condition of apathy, stupor and coma, death following by failure of the respiration. These later symptoms succeed each other rapidly, death occurring within 24 to 48 hours after the first sub-acute symptoms.

Very similar symptoms were obtained in rats. The symptoms were the same whether the drug was given hypodermically or by the mouth. *Post-mortem* appearances varied a good deal in different animals. There was often found an unusual amount of fluid in the abdominal cavity, sometimes of a bright yellow colour. Small ecchymoses were sometimes found in the omentum, and fat deposits in the abdomen. The stomach contained black masses of half-digested blood, and the duodenum also contained some effused blood mixed with mucus. The liver was swollen and congested, and the gall-bladder was generally distended with very dark-coloured viscous bile, which could only be expressed from it with difficulty. Small hæmorrhages were often found in the lungs, pancreas, kidney, and some other organs.

Dr. C. Bolton kindly examined some of the organs microscopically and found marked congestion and hæmorrhages in the liver, the hæmorrhages being in most cases confined to the peripheral half of the lobules. The hepatic cells in the centre of the lobule were often normal, but further outwards they became distorted by the blood cells and stained badly, and towards the interlobular vein they were quite colourless and evidently in process of disintegration. Large areas of necrosis of the liver were found. In acute poisoning the liver cells often contained globules of fat. There was some infiltration of round cells round the portal canal, especially involving the smaller bile ducts and extending upwards from them between the liver cells. This feature was present in sub-acute cases, though it was more marked in chronic poisoning.

In chronic poisoning no symptoms, except loss of weight, were elicited until the drug had been given for over a month. The animal then died with the same appearances as in sub-acute poisoning. *Post mortem* the pyloric end of the stomach contained a quantity of black clotted blood, the duodenum had excessive mucous secretion, the liver was found in an advanced

state of degeneration, most cells having disappeared and the few remaining staining badly. The greater part of the section was occupied by blood corpuscles in a state of decomposition. Round the vessels there were masses of round cells which appeared to be in process of change to connective tissue. The round cell infiltration extended also into the remains of the lobules and between the surviving liver cells. The cirrhosis had not proceeded so far as is described in cattle, but was of the same nature, and on the other hand was an obvious development of the process seen in animals which died from a single dose of the alkaloid.

The two alkaloids sent to me induced the same symptoms and the same changes, and seem to be equally toxic. The whole of the symptoms appear to arise from two different effects, one of them being an action on the central nervous system resembling that seen in many convulsive poisons, but this action is only induced by very large quantities. On the other hand, when smaller quantities are given, the dominating effect is hæmorrhage, which may occur in almost any organ, but which is constant in the liver and almost invariably present in the stomach and bowel. The hæmorrhage in the liver appears to be the cause of most of the other changes, such as the dropsy and jaundice, and the destruction of the liver cells appears to be the starting point for the cirrhosis. Together with the hæmorrhages in the stomach the hepatic changes may probably be the explanation of the loss of weight which forms a characteristic feature in chronic and sub-acute poisoning.

The results with the alkaloids of the *S. latifolius* suggested the examination of the action of the *S. Jacobœa* in this country. Inquiries in various parts of this country indicated that poisoning with this plant is unknown. In accord with this, I have been unable to obtain any symptoms from animals in which large quantities of the extract of the English ragwort were injected. On the other hand, the same plant growing in Canada has been shown to induce the characteristic cirrhosis, but an extract of a quantity of this plant grown in Canada also proved inactive. It is possible, however, that the plant from which my preparations were made had been collected at the wrong season, or the alkaloids may have undergone changes into some inert form in the course of preparation.

S. silvaticus collected in Yorkshire in August proved equally inactive. *S. vulgaris,* or common groundsel, collected in England and prepared in the same way, proved poisonous, the animals dying from symptoms resembling those arising from senecifoline, but with marked diarrhœa.