

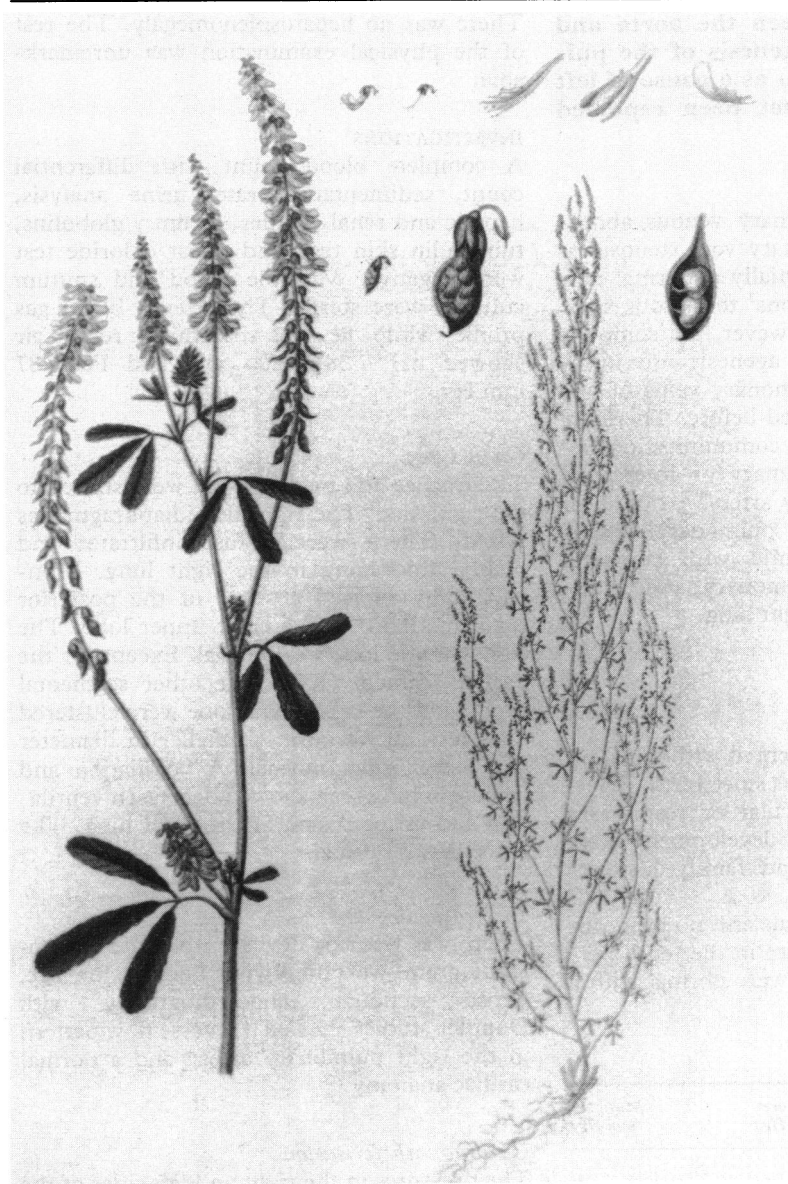
been recorded. Initial attempts at surgical excision were associated with a high mortality; however, the use of cardiopulmonary bypass and advances in technique have dramatically improved the safety of this procedure.¹⁰

This rare but important condition should be considered in patients of African origin in the clinical differential diagnosis of mitral valve disease and in the echocardiographic differential diagnosis of masses apparently within the left atrium.

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PLANTS IN CARDIOLOGY



Melilotus officinalis (L.)
Lam. *Flora Danicae*
1787: volume vi; plate
934.

Dicoumarol and warfarin

The poor soil, low rainfall, and hard winters of the North American prairies made it difficult to grow crops for animal feed until the melilots or sweet clovers, *Melilotus alba* and *M officinalis* (Leguminosae), were introduced from Europe early this century. They did well and were used

for winter feed. In 1922 a new and mysterious disease of cattle was reported in Alberta by a veterinary surgeon F S Schofield who noted that cattle fed on mouldy sweet clover hay were dying of haemorrhage. Properly cured hay was harmless. Schofield found that the clotting time was prolonged: a few years later L M Roderick a veterinary surgeon in Dakota showed that this was due to a reduced crude prothrombin fraction in the blood. The coincidental introduction by Dr A J Quick of his one stage prothrombin method proved essential for further progress. Dr K P Link, who worked in Wisconsin where the disease was common, then took up the search for the enigmatic "haemorrhagic agent". It was six years before the agent was isolated in his laboratory by H A Campbell at dawn on 28 June 1939. It was shown to be a derivative of coumarin—the substance that gives a sweet smell to new mown hay—and was named bishydroxycoumarin. It is formed by fungal action in mouldy sweet clover by oxidation of coumarin to 4-hydroxycoumarin which is then coupled with formaldehyde. On 1 April 1940 it was synthesised. It was first used clinically as an oral anticoagulant at the Mayo Clinic in 1941. The American trade name was dicoumarol; and this was adapted in Britain to become the official name dicoumarol.

Link got tuberculosis in 1945 and, having unsuccessfully tried out dicoumarol as a rat poison in 1942, he spent six months in the sanatorium reading about the history of rodent control. From 1946 to 1948 his laboratory staff reappraised the synthetic coumarin derivatives that they had made and found that number 42 had a potent and uniform anticoagulant action. Link proposed it as the ideal rodenticide and coined its name warfarin from the Wisconsin Alumni Research Foundation, which had promoted its use, plus the suffix from coumarin (*Circulation* 1959;19:97-107). Though dicoumarol was enthusiastically used by clinicians warfarin, a rat poison, was ignored—until an army recruit failed to commit suicide after taking a huge dose. Warfarin was soon shown to be better and safer than dicoumarol. It was introduced into clinical practice in 1954.

A HOLLMAN