

cases, and aspiration biopsy proved helpful in the diagnosis in cases 2 and 3. Necropsy confirmed the presence of a primary bronchial carcinoma in case 1. In cases 2 and 3 it seems probable that the primary lesion was a carcinoma of the bronchus, in view of the evidence of lung involvement and of the histology of the biopsy material in case 2.

In cases 2 and 3 there was a delay of six and of eight weeks between the onset of symptoms caused by the bony metastases and the appearance of signs of pulmonary involvement. Such a delay is by no means uncommon; Hirsch and Ryerson (1928) described two cases in which the delay was six and sixteen months.

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VITAMIN E IN ANGINA PECTORIS

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It has been suggested (Vogelsang and Shute 1946) that vitamin E relieves the pain and improves the exercise-tolerance of patients with angina pectoris. Shute (1942) observed that this drug dilated the local capillaries in senile vulvitis, and he suggested that in angina pectoris it acted as a coronary vasodilator. An alternative hypothesis, supported by the independent experimental work of Govier et al. (1946), was that vitamin E had a beneficial influence on the metabolism of cardiac muscle.

Sudden death has been noted in cattle with a deficiency of vitamin E (Gullickson and Calverley 1946). This was attributed to cardiac damage, and in one animal electrocardiography showed changes in the P-R interval, low-voltage prolonged QRS complexes, and changes in axis-deviation. Atrophy and scarring of the cardiac muscle, with increase in the cellular elements, were found at necropsy. Supporting this hypothesis is the observation that animals with muscular dystrophy, artificially induced by diets deficient in vitamin E, die of cardiac failure. The published work on this subject, however, is not critical, nor are the observations adequately controlled, and the questions asked in the *British Medical Journal* (1946) regarding the efficacy of vitamin E in angina pectoris led us to carry out a clinical trial.

Our series consisted of twenty-two patients (17 men and 5 women), aged 44-66, and our technique was based on that of Evans and Hoyle (1933), only patients having frequent attacks of typical anginal pain being included. All had a negative Wassermann reaction, and patients with thyrotoxicosis or with a haemoglobin less than 90% (Haldane) were excluded. Because of the possible occurrence of further small thromboses which might influence our results, no patient who had clinical or electrocardiographic evidence of coronary thrombosis in the previous six months was included.

Patients received vitamin E ('Ephynal,' Roche) 50 mg. t.d.s., or phenobarbitone gr. $\frac{1}{2}$ t.d.s., or aminophylline 0.1 g. t.d.s., or calcium lactate gr. 5 t.d.s. (as a

control). Since 90 mg. of α -tocopherol acetate a day has been shown to raise the blood level, the dose we used should have been sufficient to produce therapeutic effects. Each drug was given for three weeks, and the patients were seen at the end of each period. They did not know which of the drugs they were taking; nor was the order of administration the same in each case. All other therapy ceased during the period of investigation.

A detailed history of the factors causing pain was taken in each case, and the frequency of attacks was

TABLE I—EFFECTS PRODUCED BY DIFFERENT DRUGS ON ANGINA PECTORIS

Result	Vitamin E	Phenobarbitone	Aminophylline	Calcium lactate
Better ..	10	10	8	4
No change ..	6	8	8	9
Worse ..	6	4	6	9

estimated. At each subsequent visit the patient was questioned about changes in frequency or precipitating factors, any unusual symptoms which could be ascribed to the drug were noted, and the patient was asked to give his opinion of the effect of the drug on his general condition. At the end of the investigation the patient was asked which of the drugs produced the greatest benefit.

The results shown in table I suggest that vitamin E is no more beneficial than phenobarbitone or aminophylline, and our observations support the conclusion of Evans and Hoyle (1933) that none of these drugs is of much value in the routine treatment of angina pectoris. Table II suggests that phenobarbitone is the most useful and diminishes the liability to anginal attacks, as suggested by Bramwell and King (1942). Among the patients who found vitamin E the most beneficial no common factor was noted in the electrocardiogram, blood-pressure, age, blood-cholesterol, length of history of the disease, size of heart as measured in the tele-radiogram, or family history.

As regards possible toxic manifestations of vitamin E, one patient complained of a dry feeling in the throat, two had increased headaches, and one noted pronounced

TABLE II—DRUG PRODUCING MOST BENEFIT IN ANGINA PECTORIS

Patients	Vitamin E	Phenobarbitone	Aminophylline	Calcium lactate
Men (17) ..	6	8	3	0
Women (5) ..	0	2	1	2

vasodilator effects in the form of flushing of the face, throbbing headaches, and giddiness.

SUMMARY

Twenty-two patients with typical angina of effort were treated with vitamin E, phenobarbitone, aminophylline, and calcium lactate, each drug being given for 3 weeks, after which the patients were asked to compare the effects of the drugs.

From this small but clinically significant series it is concluded that vitamin E is not of any therapeutic value in the routine treatment of angina pectoris.

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