Miss E. Quilley for technical assistance and to the Board of Governors of King's College Hospital for grants towards the cost of the work from their endowment funds.

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THROMBOSING ARTERIOSCLEROSIS RESULT OF LONG-TERM ANTICOAGULANT THERAPY

BY

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Man lives with arteriosclerosis, and dies of the complicating thrombosis. The combination represents a disease entity which should be called "thrombosing arteriosclerosis." The symptoms depend on the seat of thrombosis—giving angina pectoris or coronary infarction, cerebral accidents, or intermittent claudication—and the prognosis is first and foremost the prognosis of arteriosclerotic heart disease.

Thrombosing arteriosclerosis is confined to man alone. We are not able therefore to produce the disease in experimental animals, because they cannot achieve thrombosis spontaneously even if some part of the coagulation system may be influenced during experiments with hypercholesterolaemia in animals (Dedichen, 1950).

Since 1950 I have been giving long-term anticoagulant therapy to out-patients with arteriosclerosis, 149 of whom have been under constant treatment for one year or more (Table I). This report gives the results of treatment with phenindione ("phenylindanedione"), using a method described elsewhere (Dedichen, 1953).

TABLE I.—Number of Cases and Duration of Treatment

	No. of Patients	Months of Treatment	Average Length of Treatment
Coronary thrombosis or angina pectoris	86	2,693	31 months
Intermittent claudication	63	2,016	32 "
Total	149	4,709	31.6 "

Results and Treatment

Of 86 patients with coronary disease, 12 died during the period of observation (Table II), giving a mortality rate of 5% a year. This is in conformity with the results of Owren

(1954, 1955), who since 1949 has been treating coronary thrombosis and angina pectoris with long-term anticoagulant therapy, and whose results have been confirmed by Bjerkelund (1956). Among the 63 patients with intermittent claudication in this series eight deaths occurred during the period of observation—that is, 5% a year.

TABLE II.—Cause of Death

	Coronary Thrombosis or Angina Pectoris	Intermittent Claudication
Sudden death	5	6*
Coronary thrombosis	2	
Heart failure	2	
Cancer	1	1
Other causes	2†	1 (suicide)
Total	12	8

* One died fourteen days after cessation of two years' therapy.

† One died fourteen days after cessation of therapy, owing to bleeding from gastric ulcer.

The main cause of death was arteriosclerotic heart disease. Of the patients with intermittent claudication, 54% had clinical signs or symptoms of arteriosclerotic heart disease when treatment was started, or developed such signs during the period of observation. It is therefore difficult to establish the group to which the particular patient belongs. I have followed the rule that the symptoms which bring the patient to the clinic for treatment have been definite. The two groups correspond closely as regards mean age, blood pressure, and cholesterol values (Table III); but there is a greater frequency of women in the coronary group. Diabetes occurred in only three of the 149 cases.

Complications.—Severe haemorrhage necessitating admission to hospital occurred six times: haematemesis, twice (once gastric ulcer); gross haematuria, three times; and haemoperitoneum once (from regional ileitis). Nose bleeding was also a complication. Slight haematuria has not been of importance and is not recorded. Six patients out of a total of 200 treated have shown signs of sensitization to phenindione, with rash, and have been switched over to dicoumarol.

TABLE III*

	No. of Patients			Cholesterol (mg./100 ml.)	B.P.	Average Age
	M	F	Total			
Coronary thrombosis or angina pectoris	86	15	106	280	150/90	57.5
Intermittent claudication	63	4	80	278	160/90	58.3

* This includes 37 cases on long-term treatment.

Comments

The prognosis of intermittent claudication is difficult to establish with certainty. The selection of material will of course influence the mortality, and here the percentage of complicating diseases, such as diabetes, is of great importance. Of 280 patients at the Mavo Clinic (Allen, Barker, and Hines, 1946), 116 were followed up after three years and showed a mortality of 54.6%, 20% had diabetes, and 70 had undergone amputation. Six of my patients had chronic ulcers—five being healed during treatment—and one underwent amputation.

The beneficial effect of anticoagulant therapy is thought to be due to the prevention of further intravascular thrombosis, giving time for development of collaterals. Other pharmacological effects of the anticoagulants have not been recorded.

Other factors which may influence the course of the disease are exercise, diet, and smoking habits.

Exercise.—The modern treatment of arteriosclerosis is a more active concept, the patient being encouraged to take exercise. This view is probably to some degree due to

observations on London Transport workers made by Morris *et al.* (1953)—which showed that the mortality of coronary thrombosis is higher in the group of employees with less activity (drivers in comparison with conductors)—and on London postmen. Our patients are instructed to take daily exercise, if possible one hour's walking a day, and to try to accelerate the speed up to (but not beyond) the point where they are forced to stop or slow down.

A 52-year-old officer was able to walk at a speed of 30 steps a minute at the start of treatment. After two years' treatment he could walk at 110 steps a minute.

Diet.—The patients have been encouraged to reduce their weight and avoid heavy meals, particularly fatty ones. The following case illustrates the role of fat and of exercise in arteriosclerosis.

A 36-year-old man spent his holidays in the mountains (Hardangervidda) the year after the liberation. There he met friends from the resistance movement—farmers who had assisted in taking care of sabotage groups during the war. He was overwhelmed with all sorts of dairy produce, which had been so scarce for years. During his three weeks' stay (taking long hikes almost every day and getting a lot of exercise) he developed thrombosis of the abdominal aorta, which was almost completely obliterated. He has since got coronary disease as well. There are no signs of Buerger's disease or of familial cholesterolaemia.

The role of the diet as compared with the importance of exercise has been commented on in another observation (Dedichen *et al.*, 1951). The frequency of thromboembolism after operation declined during the war and rose again afterwards. Here exercise must be left out of the picture.

Tobacco.—Many patients have been heavy smokers, but their smoking habits have not been recorded with such consistency as to form a background for further comment. About half the patients have stopped smoking. There have been difficulties in persuading patients to stop smoking, particularly in the elder group. Some have stopped for more than a year without showing any improvement in the condition.

Summary

The mortality rate in a series of 149 out-patients with thrombosing arteriosclerosis on long-term treatment with anticoagulants has been shown to be 5% a year.

It makes no difference whether the process is localized to the heart or to the arteries of the limbs.

I thank Nyegaard and Co., Ltd., of Oslo, for supplies of phenylindanedione.

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The advances made during the last decade in educating blind, deaf, epileptic, and similarly handicapped children are reported in *Education of the Handicapped Pupil* (Ministry of Education Pamphlet No. 30, price 2s., H.M.S.O.). "Between January, 1946, and January, 1955," the pamphlet reports, "the number of special schools increased from 528 to 743, the number of pupils in them from 38,499 to 58,034, and the number of full-time teachers from 2,434 to 4,381." One-year training courses for teachers of educationally sub-normal children are held by London, Birmingham, and Leeds Universities: Manchester University's Department of Education of the Deaf can now take 65 students yearly; and Birmingham hopes to open a training course for teachers of the blind in 1956–7.

EYE INJURIES DUE TO FIREWORKS

BY

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In an attempt to ascertain the number of eye injuries due to fireworks on November 5, 1955, seventy hospitals with eye out-patient departments in the London postal area were circularized. The ophthalmic registrar or deputy was asked to give details of patients who, as a result of accidents with fireworks, sustained eye injuries which necessitated their admission to hospital. Forty-four replies were received, which included those from all the London teaching and ophthalmic hospitals. It was felt that details of minor injuries not requiring in-patient treatment would be difficult to obtain, but the replies contained information relating to 25 such injuries, including the case of a man whose cornea was scratched while rescuing a cat frightened by fireworks.

Details of Injuries

Fourteen people, all male, between the ages of 3 and 46 suffered major eye injuries (see Table). These can be divided into two groups—that is, those due to flash burns and those due to direct injury by the firework.

Summary of Eye Injuries Due to Fireworks on November 5, 1955, in the London Postal Area

Case	Age	Sex	Type of Injury	Mode of Injury	Result
1	7	M	Superficial burns of right eye and lids	Exploding firework	No permanent damage
2	14	M	Superficial burns around eyes and lids	Making fireworks at home	" "
3	7	M	Severe contusion of globe. Iridodialysis, hyphaema	Struck in eye by firework	Permanent damage
4	11	M	Superficial burns of lids and cornea	Exploding firework	No permanent damage
5	14	M	Corneal staining, commotio retinae	" "	" "
6	37	M	Perforated cornea. Prolapsed uveal tissue and vitreous (previous retinal detachments)	? Hit by rocket	No perception of light in injured eye
7	12	M	Hyphaema, commotio retinae, small vitreous haemorrhage	Lighting one firework from another	No permanent damage
8	14	M	Bilateral, superficial corneal abrasions. Corneal F.B.s	Firework blew back into face	" "
9	46	M	Ruptured globe with prolapsed tissue, laceration of lid	Hit by falling rocket stick	Excision of eye
10	3	M	Superficial burns of face, corneal abrasions and F.B.s	Firework exploded in face	No permanent damage
11	11	M	Superficial burns of face, large corneal abrasions	Exploding firework	" "
12	20	M	Burns to lids and conjunctiva, corneal abrasions and F.B.s	Making fireworks with red phosphorus, pot. chlorate, and flour	" "
13	7	M	Superficial burns to lids and corneal abrasions	Exploding firework	" "
14	13	M	Superficial burns to both lids, superficial burns to right cornea, deep burns to left cornea	" "	Right eye normal. Permanent damage to left eye

Flash Burns.—Ten patients were admitted to hospital with flash injuries involving the eye and the skin around the eye. This is a similar type of injury to that suffered by gunners in the last war. There were superficial burns involving skin, cornea, and conjunctiva with singeing of the eyelashes, eyebrows, and hair. At the same time multiple minute foreign bodies were blown into the face, speckling