in long-term prophylaxis against urinary infection,⁹ and we used it in two patients. In unilateral disease, however, its very rapid clearance by the normal kidney may result in a poor concentration in the urine excreted by the diseased kidney. When both kidneys are diseased effective urine concentrations may be achieved only in the presence of potentially toxic serum levels. Furthermore, many of these patients have *Proteus* infection, and nitrofurantoin is usually ineffective against this organism in vivo. We therefore consider co-trimoxazole the agent of choice for use in the way we have described.

The failure of antibiotic treatment to prevent stone growth (or matrix calcification) in four of our patients underlines the need for close collaboration between the physician and the surgeon. The indications for surgery are difficult to define and may be influenced by the degree of supervision of the patient that will be possible. It should be emphasised that four patients in this series, and several others with stones and infection under our care, have had previous stone surgery. Sometimes, therefore, the problem is not whether to operate, but how many times, and this should always be borne in mind before first deciding on surgery. If the presence of infection is an indication for operation

it is logical to confirm by a localisation procedure that infection is present in the kidney. This is particularly important, since most patients with stones and urinary infection are women, and there is a possibility therefore that the stones may prove to be fortuitously associated with bacterial cystitis.

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Sudden deaths among Finnish conscripts

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Summary

The epidemiology of sudden deaths was studied among conscripts in Finland in 1948-72 (660 000 man-years) and among Finnish men aged 15-24 years in 1969-70 (900 000 man-years). The incidence of sudden deaths among the conscripts was 6.8/100 000 man-years. The onset of acute symptoms occurred during strenuous exercise in a third of the conscripts but in only a few of the other young men. Cardiovascular diseases caused two-thirds of the deaths in both groups. Sudden death tended to be more common among conscripts than among other young men during the corresponding period, but overall non-violent deaths were less common among conscripts than among other young men. On the basis of health records an attempt was made to separate the sudden deaths among conscripts from those among the controls by multiple discriminant analysis. For all practical purposes, however, the separation power proved poor.

Introduction

Sudden deaths constitute a large proportion of all non-violent deaths among young men,¹⁻⁴ but I am not aware of any prospective or controlled retrospective study of the epidemiology of sudden deaths among young men. In military service sudden deaths are accurately recorded. The aim of this study was to determine the incidence, causes, and risk factors of non-violent

sudden death among conscripts in Finland. Moreover, an attempt was made to identify conscripts with a "high" risk of non-violent sudden death.

Subjects and methods

The study population consisted of nearly 900 000 young men aged about 20 years who were Finnish conscripts in 1948-72. Nearly 660 000 man-years were covered. A sample of conscripts was used as a control group. One name out of every 500 was drawn from the register of 19-year-olds liable to be drafted in 1950, 1955, 1960, 1965, and 1970 in each of the 25 military districts in Finland. Data on the health of 97% of these men (418) were available. By the end of 1972 401 of the men had entered and performed military service and they formed the control group of conscripts.

In addition, the sudden deaths of young men aged 15-24 that occurred in 1969-70 in Finland were analysed. About 900 000 man-years were covered.

The health data on conscripts who died suddenly, the circumstances and clinical course of the acute illness, and the necropsy findings were analysed. The residence, social class, findings at initial medical examination, and use of medical services during military service were compared in the conscripts who died and their controls. A multiple discriminant analysis was performed with eight variables: (a) the number of days spent as an outpatient during military service, (b) the number of appointments with a doctor during the first 12 weeks of military service, (c) the number of appointments with a doctor during military service, (d) the number of days spent as an inpatient because of an infection during the first 12 weeks of military service, (e) systolic blood pressure at initial examination, (f) weight at initial examination, (g) social class before military service, and (h) the number of appointments with a doctor because of infection during the first 12 weeks of military service.

Finally, those who were conscripts in 1967-72 were compared with the remainder of the Finnish male population aged 15-24 (1969-70). The incidence and cause of sudden death and the possible connection of sudden death with strenuous exercise were the basis for comparison. The following definition of sudden death from disease was used⁵: "When a person not known to have been suffering from dangerous disease, injury, or poisoning is found dead or dies within 24 hours after the onset of the terminal illness, death is said to have been sudden or unexpected."

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Results

Forty-five conscripts died suddenly during 1948-72. The incidence of sudden death was on an average as low as 6.8/100 000 man-years. Nevertheless, sudden deaths constituted one-third of all non-violent deaths among conscripts during the same period. Cardiovascular diseases caused the sudden death in two-thirds of the cases (table I). The incidence of sudden death was fairly even during the first two months of military service, but the third month of service tended to be more risky than the others (table II). The onset of acute symptoms occurred in half the cases while the conscript was on duty and in the other half during leisure. In 15 cases the onset occurred during an estimated near-maximum or maximum physical exertion (table III). In 10 of these cases the underlying cause of death was an organic cardiovascular disease verified morphologically at necropsy (table IV). Five of the 45 sudden deaths occurred soon after vaccination (TAB in 2 cases, smallpox in 1, smallpox and diphtheria in 1, and diphtheria in 1), and four of these men (those who had had TAB, smallpox, and smallpox and diphtheria vaccinations) died from a myocardial or coronary cause during or immediately after a strenuous exercise. The interval between the onset of acute symptoms and the death was less than 15 minutes in half these cases of diseases of heart or great central arteries (table V). In other groups the interval between the onset of acute symptoms and death was generally over two hours.

The separation power of the multiple discriminant analysis proved poor. The possibility that a conscript who was put into the sudden death group on the basis of the multiple discriminant analysis would actually have died a sudden non-violent death during his military

TABLE I—Sudden deaths among conscripts in Finland during 1948-72

Cause of death	No	%
Diseases of heart and great central arteries:	16	36
Coronary arteriosclerosis; cardiac infarction	1	
Coronary arteriosclerosis and anomaly; cardiac infarction	1	
Coronary arteriosclerosis; coronary thrombosis	1	
Idiopathic medial necrosis of coronary arteries	1	
Coronary thrombosis NOS; drowning	1	
Coronary occlusion NOS	2	
Acute myocarditis	1	
Late effect of myocarditis	1	
Late effect of rheumatic carditis; coronary anomaly	1	
Myofibrosis NOS of heart	1	
Mitral stenosis	1	
Rupture of aneurysm in ascending aorta	2	
Hypoplasia of aorta	1	
Arterial rupture NOS in neck	1	
Cerebrovascular diseases:	13	29
Aneurysm of middle cerebral artery; subarachnoid haemorrhage	5	
Aneurysm of anterior communicating artery; subarachnoid haemorrhage	1	
Subarachnoid haemorrhage NOS	4	
Cerebellar haemorrhage NOS	2	
Cerebral haemorrhage NOS	1	
Other diseases:	16	36
Acute hydrocephalus NOS	1	
Epilepsy	1	
Acute fulminating meningococcaemia	2	
Meningococcal meningitis	1	
Phlegmonous laryngitis	1	
Acute necrosis of pancreas	2	
Abdominal purpura after diphtheria vaccination	1	
Heat stroke	2	
Unknown; acute collapse during strenuous exercise	1	
Unknown; acute cardiac insufficiency during strenuous exercise	2	
Unknown	2	
Total	45	100

NOS = Not Otherwise Specified

TABLE II—Period from beginning of military service to sudden death. Military service in Finland normally lasts 240 or 330 days

Days	Diagnostic group			Total
	Heart and central arteries	Cerebrovascular	Others	
<4	1		1	2
-7		1		1
-14	1	1		2
-29	1			1
-59	1		4	5
-89	6	4	2	12
-119	2	1	2	5
-179	3	3	2	8
-240 (-330)	1	3	5	9
Total	16	13	16	45

TABLE III—Activity at onset of acute symptoms

	Diagnostic group			Total
	Heart and central arteries	Cerebrovascular	Others	
At least near-maximum physical exertion	9*	1*	5†	15
Dancing	1			1
Swimming	1			1
Sleeping	1	2	3	6
Other circumstances	3*	9	7	19
Unknown	1	1	1	3
Total	16	13	16	45

*The amount of undigested or partly digested food in the stomach was about 0.5 l or more in one case.

†The amount of undigested or partly digested food in the stomach was about 0.5 l or more in two cases.

TABLE IV—Cause of sudden death in conscripts who suffered onset of acute symptoms during estimated near-maximum or maximum physical exertion

	No of conscripts
Coronary sclerosis	2
Coronary sclerosis and anomaly	1
Idiopathic medial necrosis of coronary arteries	1
Late effect of rheumatic carditis, coronary anomaly	1
Late effect of myocarditis	1
Myofibrosis NOS of heart	1
Arterial rupture NOS in neck region	1
Hypoplasia of aorta	1
Subarachnoid haemorrhage NOS	1
Heat stroke	2
Unknown; acute collapse during strenuous exercise	1
Unknown; acute cardiac insufficiency during strenuous exercise	2
Total	15

NOS = Not Otherwise Specified

TABLE V—Duration of acute illness from onset of acute symptoms to death

	Diagnostic group			Total
	Heart and central arteries	Cerebrovascular	Others	
Instant death	3			3
<15 min	6	1	1	8
-59 min	1	1	4	6
-1 hr 59 min	3	3		6
-11 h		5	7	12
-24 h		2	2	4
24 h, but not exactly specified	3*	1	2†	6
Total	16	13	16	45

*In one case acute illness lasted 12 hours at most; in another it lasted 2 hours at most.

†In one case acute illness lasted 15 minutes at most.

service was only 0.0003. The proportion of false-positive diagnoses was 1.5% and the number of false-negative ones 91%. In six cases a conscript in the control group was classified falsely into the sudden death group, and only four of the conscripts who did die were correctly classified into that group. Death resulted from acute myocarditis in two of these four cases, from idiopathic medial necrosis of the coronary arteries in a third, and from the rupture of an aneurysm in the ascending aorta in the fourth. At the retrospective cardiological survey, the finding on the mass miniature x-ray film of a further conscript of a ruptured aneurysm in the ascending aorta was almost diagnostic.

Although conscripts tend to indulge in physical exertion more than other young men, it was not possible to confirm that physical exertion exacerbated latent cardiovascular disorders. In a third of the conscripts who died the onset of acute symptoms occurred during strenuous physical exercise, but this was fairly uncommon among other young men. Cardiovascular disease, however, caused two-thirds of the sudden deaths in both groups. Sudden deaths tended to be more common among conscripts (5.8/100 000 man-years in 1967-72) than among other young men (3.2/100 000 man-years in 1969-70) ($0.10 < P < 0.05$). On the other hand, there were fewer non-violent deaths of all types among conscripts (16/100 000 man-years) than among other young men (35/100 000 man-years) ($P < 0.001$).

Discussion

Close inquiries are always made into sudden deaths among Finnish conscripts. Reports on the circumstances and the possible clinical findings during the acute illness are generally reliable. The necropsy rate was high in conscripts (93%) and also in other young men who died suddenly in 1969-70 (83%). Although the validity of death certificates is often questionable in retrospective studies⁶⁻¹⁰ the high necropsy rate in this study adds to their value.

Two of the conscripts not examined at necropsy died from an unexpected and clinically spontaneous subarachnoid haemorrhage. The third died of purulent meningitis caused by Gram-negative diplococci (*Neisseria meningitidis*). In these cases the cause of death was determined principally by clinical examination and lumbar puncture.

It was not possible to predict the disease that caused a conscript's death from findings at the initial medical examination or his use of medical services during his military service. The possibility of predicting a subarachnoid haemorrhage or an acute coronary attack was poor. On the other hand, it might have been possible in some cases to diagnose latent, potentially lethal myocarditis by relatively simple methods—for example, by taking an electrocardiogram of a conscript with an acute infection. The high incidence of sudden deaths in the third

month of military service might have been due to the combined effect of infection waves and strenuous exercise; exercises at that time tended to be more strenuous than at the beginning of service. Rules about exercise—adequate training, no strenuous exercise immediately after a meal, no strenuous exercise in excessive heat, adequate pauses, etc—should be observed.

Strenuous exercise might be risky for up to two weeks after vaccination, when a latent myocardial or coronary involvement induced by vaccination may be present. A study is in progress to investigate whether any signs pointing to cardiac disease can be shown after vaccination.

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Endotoxaemia and renal failure in cirrhosis and obstructive jaundice

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Summary

An investigation into the possible role of endotoxins in the pathogenesis of renal failure in cirrhosis and obstructive jaundice showed the two to be closely related. None of the patients with cirrhosis who had endotoxaemia had other evidence of Gram-negative infection at the time of the study, and the endotoxaemia was therefore probably due to impaired hepatic clearance of toxins normally absorbed from the gastrointestinal tract. In contrast, bacteriological evidence of Gram-negative infection was found in most of the patients with obstructive jaundice and endotoxaemia.

Introduction

Renal failure eventually develops in up to 85% of patients with cirrhosis¹ and in one series was the immediate cause of death in 11%.² In many of these patients renal tubular function and structure are maintained, and the lesion is therefore often referred to as "functional renal failure." In others an acute tubular

necrosis is found. The necrosis may have been preceded by functional renal failure. Both varieties of renal failure may arise spontaneously or be precipitated by major bleeding or infections.

The pathogenesis of functional renal failure is generally thought to be an intense constriction of the renal and intrarenal arterial vessels.³ This has been attributed to sequestering of blood in the splanchnic venous circulation as a result of portal hypertension, so that the arterial circulation is "underfilled." But Ring-Larsen *et al*⁴ were unable to find an increase in renal blood flow after successful shunt operations in six patients with cirrhosis. Another possibility is that it is due to a circulating renal vasoconstrictor substance. Endotoxins are potent renal vasoconstrictors and we have previously shown a correlation between endotoxaemia and the occurrence of renal failure in fulminant hepatic failure.⁵

Renal failure is also a well-recognised complication of biliary obstruction. One mechanism for this may be an increased renal sensitivity to the effects of anoxia.⁶ Wardle has also suggested that endotoxaemia may be important since rats readily develop renal failure after intravenous administration of endotoxin if the bile duct has been ligated.⁷ He has also reported a 25-75% incidence of endotoxaemia in patients with biliary obstruction, although details of renal function were not given.⁸

We describe here the relation between endotoxaemia and renal failure in 45 patients with cirrhosis and 12 with obstructive jaundice.

Patients and methods

CIRRHOSIS

Twenty-five of the 45 inpatients with cirrhosis had renal failure, and their plasma urea and creatinine concentrations were raised

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