Our study suggests that those sociocultural and epidemiological factors which help reduce clustering of cases and intensive exposure may help to reduce mortality from measles. Decline in deaths may occur irrespective of concurrent improvements in nutritional state, hygienic conditions, and therapeutic practices or changes in the age composition of patients.

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SHORT REPORTS

Delays in diagnosing and treating bladder cancer

Wallace and Harris said over 20 years ago that most of the responsibility for the delay in diagnosing bladder cancer lay with the hospital service.¹ I conducted this study to see whether delays still exist and, if so, where they occur.

Patients, methods, and results

All patients in whom a new bladder cancer had been found were interviewed to establish the date of their first symptom and the date of their first visit to their general practitioner for that symptom. The dates of outpatient appointments and cystoscopy were also recorded. Consultants used different methods in managing patients, and as the numbers were skewed the values given are medians (and ranges).

One hundred patients were interviewed, of whom 70 were men. The patients' mean age was 67.7 (SEM 1.27) years (range 29-92). Painless haematuria was the presenting symptom in 67, painful haematuria in 18, "cystitis" in 12, and obstructive symptoms in three. Twenty of the patients were admitted as emergencies.

The median total delay in diagnosis was 18 (1-316) weeks; the median delay by patients was 1 (1-263) week, by general practitioners 2 (1-308) weeks, and by hospitals 8 (1-226) weeks. When the 20 emergency admissions were excluded from the hospital figures the delay was 9 (2-226) weeks. The table shows the delays by sex, age, and presenting symptom.

Patients had to wait 18 (1-97) days for their first appointment at the outpatient department. Half of them were given follow up appointments, for which they waited 26 (14-82) days. The waiting time for operations was 28 (2-177) days. The time waited for the first appointment did not vary except with age: patients aged over 80 were seen in 8 (1-44) days whereas those aged under 50 were seen in 19 (15-63) days.

Comment

The patients saw their general practitioners quickly after discovering their first symptoms. This pattern has not changed over 20 years^{1,2} and is similar to that in Denmark.³ The proportion of patients presenting with painless haematuria has fallen from that of 80% reported in Bristol and London 20 years ago.^{1,2} Why more patients are presenting with confusing symptoms is

Delays in diagnosis in weeks by age, sex, and presenting symptoms. Values are medians (ranges)

	Delay			
	Overall	By patients	By general practitioners	By hospitals*
Age (years)				
<50 (n=9)	22 (5-164)	7 (1-52)	8 (1-154)	7 (2-17)
50-65 (n=28)	18 (3-267)	1 (1-263)	4 (1-178)	9 (2-88)
66-80 (n=44)	17 (4-316)	2 (1-113)	3 (1-308)	10 (2-226)
>80 (n=19)	17 (2-83)	1 (1-82)	2 (1-52)	8 (2-15)
Sex:				
Male (n=70)	18 (2-316)	2 (1-263)	2 (1-308)	10 (2-226)
Female (n=30)	16 (2-188)	1 (1-113)	4 (1-154)	7 (2-133)
Presenting symptom:				
Painless haematuria (n=67)	17 (2-316)	2 (1-263)	1 (1-308)	7 (2-226)
Other (n=33)	23 (2-133)	2 (1-52)	4 (1-52)	10 (2-133)

* Excluding emergency admissions.

unclear. Patients under 50 delayed longer than older patients, for which no discernible reason could be found.

General practitioners responded well to patients presenting with painless haematuria: three quarters of them referred such patients within a month. This is an improvement over the past 20 years.¹ General practitioners tended, however, to delay longer in referring patients under 50.

The time taken by the hospital service was disappointing. Wallace and Harris said that the median delay in the hospital service was around seven weeks and this has now increased to nine, partly because of differences in patterns of referral. The delay in Denmark, however, was three weeks.³ Although disagreement exists about whether a delay in treatment alters the prognosis,^{1,3} any delay is obviously worrying for patients and their relatives. I could not easily identify any particular factor causing this delay. One reason is probably inflexibility. As more patients are seen each year clinics and operating lists become fully booked sooner, leaving little opportunity to add urgent cases. Various administrative errors conspired to delay admissions. In addition, one of the consultants ran a clinic for haematuria in these hospitals, the effect of which was to reduce the delay till the first appointment, though it had no effect on the overall delay.

This study highlighted the need for audit of routine hospital practice; subsequently efforts were made to improve the service.

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Response to D-Trp-6-luteinising hormone releasing hormone (Decapeptyl) microcapsules in advanced ovarian cancer

D-Trp-6-luteinising hormone releasing hormone and other gonadotrophin releasing hormone agonists are proving useful in treating benign and malignant disease.^{1,2} We describe 39 patients with advanced ovarian cancer who were treated monthly with a long acting depot preparation of D-Trp-6-luteinising hormone releasing hormone.

Patients, methods, and results

Approval of the local ethical committee was obtained, and all patients gave informed consent. There were no specific exclusion criteria. All patients had a clinical examination with a full range of haematological and biochemical tests including assays of carcinoembryonic antigen, luteinising hormone, follicle stimulating hormone, prolactin, and 17 β -oestradiol, and radiological investigations. These tests were repeated at follow up. Standard criteria of the International Union Against Cancer were used to assess clinical response.

All 39 patients (mean age 61 (range 42-79)) had a poor prognosis (International Federation of Gynaecology and Obstetrics grade III (31 patients) or IV (eight) disease) and a poor performance state (40% on the Karnofsky performance index). The main sites of disease were pelvic or abdominal tumour (31), lymph nodes (five), metastases or effusion in the lung (five), liver metastases (eight), and ascites (12). Previous treatment comprised radiotherapy (29), chemotherapy with cisplatin or an analogue (35), and other chemotherapy (two); two had not had chemotherapy. The table shows the hormonal response to treatment. The mean oestrogen concentration was <70 pmol/l before treatment and did not change significantly, but the concentration of gonadotrophins was significantly reduced at one month and subsequently throughout treatment ($p < 0.001$). Fifteen patients developed intestinal obstruction within the first eight weeks of treatment and continued to deteriorate. Six had severe intestinal obstruction at the start

Mean (SEM) hormonal response to treatment

	Follicle stimulating hormone (U/l)	Luteinising hormone (U/l)	17 β -Oestradiol (pmol/l)
Before treatment	33.0 (0.8)	29.7 (0.8)	<70
After:			
1 Month	3.6 (0.1)	4.2 (0.3)	<70
3 Months	3.2 (0.1)	2.7 (0.1)	<70
6 Months	3.3 (0.2)	2.8 (0.2)	<70
12 Months	3.4 (0.4)	3.5 (0.1)	<70

of treatment, of whom one responded dramatically to treatment: her intestinal function returned to normal at three months and remained normal at six months.

Six patients achieved partial remission (overall response rate 15%). The longest remission (>18 months) occurred in a patient with a large abdominal mass. Five patients remained stable during treatment; they received the drug from six to 12 months. In 28 patients the tumour progressed; 25 of these patients died within the first 16 weeks. Mean survival was significantly longer in the six patients who responded (10 months (range six to 18)) than in those who did not ($p < 0.05$, unpaired t test). Response did not correlate with histological subtype or grade of cancer, and the histological findings were not significantly different in patients who responded and those who did not. Those who responded were older, and the natural course of their cancer seemed to be slower as most of them had had their disease for several years before the start of the study.

The drug was free of side effects.

Comment

Recently, luteinising hormone (human chorionic gonadotrophin) receptors were identified in tissue from ovarian cancers, and experimental studies showed increased growth of cell lines of human ovarian cancers treated with commercial luteinising hormone (human chorionic gonadotrophin) from the urine of pregnant women. Gonadotrophins have also been implicated in ovarian carcinogenesis.³ High capacity binding sites for luteinising hormone releasing hormone have been identified in tissue from ovarian cancers.⁴ The physiological role of these receptors is not known, but they may be one mechanism by which agonists of luteinising hormone releasing hormone inhibit growth of tumours. The predominant mechanism of action, however, is probably through suppression of gonadotrophins.

In a study in which patients who had relapsed after treatment with melphalan were given combination chemotherapy (including cisplatin) the response rate was only 30%.⁵ When cisplatin has been used as first line treatment response rates are even lower. This is similar to our results, although our patients generally had a worse prognosis. D-Trp-6-luteinising hormone releasing hormone is safe and useful for treating advanced ovarian cancer and can be recommended for patients who have relapsed after chemotherapy and those who cannot tolerate chemotherapy.

D-Trp-6-luteinising hormone releasing hormone (Decapeptyl) microcapsules for injection were kindly supplied by Ipsen International, 75016 Paris, France.

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