(5–126 μg/l), Fig. 1. The time from the sampling to diagnosis ranged from 4 to 176 months. 7 of the 31 persons who developed cancer had samples taken less than 2 years prior to diagnosis; 6 of these had PSA values > 4 μg/l, Table 1.

With a matched analysis an odds-ratio of 24 was obtained comparing those who had PSA > 4 μg/l with the persons having PSA ≤ 4 μg/l, (95% confidence interval, 3.1–185; $P = 0.002$). This means that men with serum PSA > 4 μg/l have a 24 times higher risk of having a prostatic cancer diagnosis compared with those who have values ≤ 4 μg/l. One person who developed cancer had samples taken twice. The concentration was increasing with PSA values of 8 and 20 μg/l in samples taken 26 and 15 months prior to diagnosis, respectively.

This study was performed to evaluate the usefulness of the Janus serum bank and to look for appearance of PSA in serum prior to diagnosis of prostatic cancer. The validity of such investigations depends on appropriate control groups. The Red Cross blood donors allow this possibility. The long interval from sampling to diagnosis, may reflect that prostatic cancer usually affects men at advanced age, and they simply stop donating blood before this age.

Our essential finding is the difference in PSA levels between the case and the control group, leading to a significantly increased probability of later getting a diagnosis of prostate cancer if the PSA value is > 4 μg/l. Our data support previous results [7] that elevated serum PSA identifies patients at high risk, and that this cancer can be detected by PSA measurements years before the clinical diagnosis is established.

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Haemorrhagic Cystitis Requiring Cystectomy After Cyclophosphamide and Radiotherapy

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HAEMORRHAGIC CYSTITIS is a well recognised complication of cyclophosphamide therapy. Hepatic microsomal activation of the parent compound leads to the production of active alkylating metabolites and acrolein, and urinary excretion of these products causes damage to the urothelium. Following intravenous doses of 1 g/m^2 or less of cyclophosphamide, the maintenance of a urine output of at least 100 ml/h prevents urotoxicity; with larger doses or with pre-existing urinary disease, uroprotection with mesna is recommended. The late effects of cyclophosphamide on the bladder include fibrosis and secondary carcinoma. We present a case in which substantial bleeding from the bladder, precipitated by irradiation, occurred 5 years after chemotherapy for non-Hodgkin's lymphoma.

A 35-year-old woman presented with a painful mass in the distal femur, biopsy of which revealed diffuse centrocytic centroblastic non-Hodgkin's lymphoma. Computerised tomography (CT) suggeted a nodal mass on the right side of the pelvis. A bone marrow trephine biopsy from the ilium was normal, and the patient had no systemic symptoms. Chemotherapy was commenced comprising cyclophosphamide 1 g/m^2, epirubicin 60 mg/m^2, and vincristine 1.6 mg/m^2, q3/52, and oral prednisolone 50 mg daily. After two courses of chemotherapy there was dramatic resolution of the primary lesion. Concomitant radiotherapy and chemotherapy was administered over 1 month: the patient received 300 mg/m^2 cyclophosphamide and 1.6 mg/m^2 vincristine at weekly intervals, and radiotherapy, 45 Gy in 20 daily fractions, to the distal femur. This was followed by a further four courses of cyclophosphamide, epirubicin and vincristine. A CT scan showed complete resolution of the primary tumour but the mass in the right pelvis was unchanged, and was attributed to a simple ovarian cyst.

Over 2 years the patient remained well, but during the next 6 months the pelvic mass increased in size, reaching 5 × 7.5 × 10.5 cm before laporotomy was performed. At operation tumour was found replacing the right ovary, and the histology of this was identical to her original lymphoma. The left ovary and uterus were free of tumour and a paraaortic node biopsy was negative, but peritoneal washings contained malignant lymphoid cells. Postoperative radiotherapy was delivered to the whole abdomen and pelvis: the abdominal cavity received a dose of 22.5 Gy in 20 daily fractions, with renal shielding after 13.5 Gy, and the pelvis received 45 Gy in 30 daily fractions. Two years later the patient was admitted with profuse

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haematuria. At cystoscopy the entire bladder mucosa was ulcerated and the bleeding was not controlled by diathermy. After transfusion of a total of 14 units of blood, a cystectomy was carried out. Histological examination of the bladder revealed no tumour but extensive oedema and focal erosion of the mucosa in keeping with the clinical diagnosis of haemorrhagic cystitis.

This case demonstrates two points of interest. Differential responses at a number of sites may follow chemotherapy, and in haematological malignancies are usually attributed to limited drug access to 'sanctuary sites', notably the central nervous system, the eye, and the testis. There is no evidence that the ovary enjoys such protection from cytotoxics and it must be presumed that the ovary contained drug-resistant lymphoma in this case. It is curious that this tumour did not disseminate during 2½ years without treatment. The time course and the severity of the haemorrhagic cystitis are also unusual. The dose of cyclophosphamide received was moderately high, but there was no haematuria during the patient's chemotherapy. Clearly, there must have been subclinical urothelial damage, but in series where comparable doses of cyclophosphamide have been followed by pelvic irradiation we have not found reports of bleeding requiring cystectomy [1, 2]. The combination of cyclophosphamide and pelvic irradiation, however sequenced, is potentially damaging to the bladder, and it may be appropriate to consider the use of mesna uroprotection in situations where cyclophosphamide-containing regimens are likely to be followed by pelvic irradiation.

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Local Response and Long-term Results of Preoperative M-VAC Regimen in Regionally Advanced Transitional Cell Carcinoma of the Bladder

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WE REVIEWED retrospectively the effect of neoadjuvant M-VAC regimen in 17 patients with regionally advanced transitional cell carcinoma (TCC) (5T3, 12T4, 3N+) and evaluated the role of subsequent surgery on tumour control and long-term survival. Of the 17 patients 14 were male, the age of the patients ranged from 24 to 74 years with a mean of 58 years and the median Karnofsky performance status was 70. Chemotherapy was administered according to the regimen and schedule described by Sternberg *et al.* [1]. All patients received two initial courses followed by response evaluation (cystoscopy, bladder biopsies, and computer tomography scan of the pelvis). In the presence of complete response, one further course was administered followed by radical surgery. If partial response occurred, two additional M-VAC courses were given before proceeding with surgery.

Radical cystectomy was performed in all patients with no major complications. All patients were followed-up until death or for a minimum of 42 months (mean: 56, range 42–78 months). Tumour downstaging (T0, Ta, T1, CIS, N0) occurred in 4 (80%) of the 5 T3 patients, and in 3 (25%) of the 12 patients with T4 tumours.

Long-term survival with no evidence of disease was achieved in 5 out of 17 patients (30%), suggesting that this approach did not alter the ultimate course of the natural history of the disease. Although the best survival rate was achieved in those who responded locally (Table 1), this result is in contrast with the 5-year survival of 75% reported in a recent review of 147 patients [2].

Local clinical recurrence was not detected in any patient. However, 70% of the patients with downstaged cancers developed distant metastases; this figure is similar to that reported for advanced TCC of the urothelium treated with M-VAC regimen where 68% of complete response patients relapsed [3].

Although in this small series we could not identify any trend for improved survival with neo-adjuvant M-VAC chemotherapy, our observations suggest that this regimen can render locally

Table 1. Results

No. of patients	Stage		Current status*	Follow-up (months)
	Clinical	Pathological		
3	T3 Nx	pT0	NED	48+
		pT1	DOD	12
		pTCIS† N+	DOD	16
2	T3 N+	pTCIS	AWD	78+
		pTCIS	NED	42+
10	T4 Nx	pT0	NED	46+
		pTa	DOD	28
		pT3	NED	50+
		pT3	DOD	6
		pT3	DOD	16
		pT3 CIS	DOD	12
		pT3 N+	DOD	14
		pT3 N+	DOD	34
		pT4	DOD	23
		pT4 N+	DOD	10
1	T4 N+	pT3	DOD	8
1	T4 Nx M+‡	pT CIS	NED	66+

*NED: no evidence of disease; AWD: alive with disease; DOD: died of disease. †CIS: carcinoma *in situ*. ‡Solitary pulmonary nodule resected before chemotherapy.

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