Goldman and Warner[2] described a patient with haemorrhagic cystitis during cyclophosphamide therapy and cytomegalovirus (C.M.V.) infection. C.M.V. inclusions were found within endothelial cells lining ectatic vascular channels in the lamina propria of the bladder. This finding prompted us to investigate for C.M.V. infection in another patient with haemorrhagic cystitis during cyclophosphamide therapy.

A 63-year-old man had been treated by X-irradiation for a superior-vena-cava syndrome due to reticulosarcoma. Afterwards he had been receiving cyclophosphamide in daily doses of 100 to 150 mg. during 37 months, when haematuria emerged. Intravenous urography showed no abnormalities. Cytoscopy (Prof. P. W. Boer), revealed a hyperaemic and easily bleeding bladder mucosa. Clear urine was seen to come out from both ureteral orifices. The platelet-count was 120,000 per c.mm. The one-stage prothrombin-time, kaolin-activated partial thromboplastin-time, and fibrogen were within normal limits. Fibrinolysis was negative. All urine cultures were negative for bacteria. C.M.V. was isolated from urine and mouth swabs. The haematuria subsided gradually and disappeared after 3 months. The patient died 6 weeks later from progressive reticulosarcoma. Necropsy findings included slightly dilated vascular channels in the bladder. C.M.V. inclusions were not found in the bladder nor in other organs.

Urinary metabolites are suggested to provoke haemorrhagic cystitis by local irritation during cyclophosphamide therapy. As such toxicity does not develop universally, an additional factor may be implicated. We agree with Goldman and Warner[2] that it cannot be concluded whether C.M.V. infection is only an incidental finding, or has contributed to the cystitis—e.g., by enhancing the susceptibility of the bladder to the effects of cyclophosphamide metabolites. Conversely, the injured bladder may have offered a preferential site of localisation for the virus. In our case, involvement of the bladder in the infectious process has not been demonstrated at necropsy, 6 weeks after disappearance of the haematuria.

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CYTOTOXICITY AFTER B.C.G. INFECTION

SIR,—We read with interest the article by Dr Fergula (Dec. 29, p. 1476) about increased cytolytic activity of liver fractions following B.C.G. infection. There exist a lot of data concerning in-vivo growth inhibition of tumour cells by B.C.G. infection,[1-4] but not much information is available about B.C.G. infection and in-vitro cell-mediated cytotoxicity. We therefore investigated the influence of B.C.G. infection in mice on cell-mediated cytotoxicity against allogenic target cells. C_{57} B1 mice were injected intraperitoneally with 5×10^6 viable B.C.G. organisms. 4 and 8 days after infection we looked for cytotoxicity of spleen and peritoneal cells against chicken erythrocytes labelled with chromium-51.[5] The reactions were performed by incubation of 1×10^5 erythrocytes and 5×10^6 spleen cells or macrophages in a total volume of 1 ml. RPMI 1640 supplemented with 10% fetal calf serum. The percentage of total activity released in supernatants after 40 hours was determined. Compared with normal mice, spleen and peritoneal cells of B.C.G.-infected animals showed an increased cytotoxic activity which was already evident 4 days after infection (see accompanying table).

PERCENTAGE OF ^{51}CR RELEASED FROM CHICKEN ERYTHROCYTES AFTER 40 HOURS' INCUBATION WITH CELLS FROM B.C.G.-INFECTED MICE

—	Spleen cells	Peritoneal cells
Normal mice	22.2±0.71 (6)	23.0±0.31 (6)
4 days after infection with B.C.G.	24.2±0.71 (3)	28.1±1.47 (4)*
8 days after infection with B.C.G.	43.7±1.63 (3)†	49.7±1.09 (4)†

* $P < 0.005$, † $P < 0.001$, compared with cells from normal mice.
Values are the mean of n cultures ± standard error of the mean. Each experimental group consisted of pooled cells from 4 mice.

Dr Fergula has found increased cytolytic activity against mastocytoma cells in liver homogenates of B.C.G.-infected mice, and presumes that this may be due to activation of mononuclear phagocytic cells. Our data support this assumption. Non-specific cytotoxic effects of macrophages to antigenically unrelated target cells have been described after experimental infection with parasites,[6,7] while cytotoxicity of peritoneal cells from B.C.G.-infected mice was reported to be demonstrable only after preincubation with P.P.D.[8,9] In our experiments spleen cells of B.C.G.-infected animals show an increased cytotoxicity almost as great as peritoneal cells. Though it is possible that this activity is partly due to spleen macrophages, the role of lymphocytes has yet to be clearly defined. Further investigations involving cell-mediated cytotoxicity may help to clarify the mode of action of B.C.G. in cancer immunotherapy.

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CHILDHOOD ENURESIS/ADULT DEPRESSION

SIR,—I have been impressed by the number of children with primary enuresis in whom a family background of endogenous depression can be elicited. Perhaps prospective studies on enuretic children, and retrospective histories from patients (or their parents) with established endogenous depression, may demonstrate a statistically significant relationship. Parents of enuretic children tell of how "deeply" their children sleep; sleep disturbances in endogenous depressions are well established.[1,2] Imipramine may benefit both conditions by a primary effect on a disturbed sleep process.[3]

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