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Escherichia coli O157 infection masquerading as 'rectal bleeding': a further problem for infection control

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Infection with *Escherichia coli* O157 can result in a range of symptoms, from mild diarrhea to severe hemorrhagic colitis [1]. The appearance of stools from patients with severe *E. coli* O157 colitis has been described as 'all blood and no stool' [2], which can be mistaken for non-infectious rectal bleeding.

We have recently seen two separate incidents where patients were admitted to our hospitals with a diagnosis of rectal bleeding and infection was not suspected. Subsequent stool cultures yielded *E. coli* O157 and isolation procedures, as per policy, were introduced only after the diagnostic delay. Further enquiry elicited a history of preceding diarrhea in both cases. In one episode, indistinguishable isolates of *E. coli* were subsequently obtained from two further patients and three members of the nursing staff on the same hospital ward, indicating cross-infection during the window period before isolation was instituted.

We are aware of other serious incidents of hospital cross-infection occurring with this organism [3]. As *E. coli* O157 has a particularly low infectious dose [1], nosocomial transmission can occur when infection control procedures are suboptimal [4]. This is more likely when staffing levels are inadequate, and patients are moved around quickly from ward to ward after admission, as happened in our second case.

We suggest that specific enquiry for a preceding history of diarrhea should be made in all cases of rectal bleeding, as this may be due to *E. coli* O157. If such a history is forthcoming, infection precautions should be taken from the start.

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Lack of efficacy of ozone therapy in HIV infection

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It has been shown that ozone promptly inactivates HIV-1 in vitro [1] and may alter surface markers in HIV-1-infected lymphocytes. However, owing either to poor methodology [2] or to multiple complementary treatments, the usefulness of ozone therapy in vivo remains questionable [3]. The advantages and disadvantages of ozone therapy in HIV-1 infection have been discussed [4], particularly with regard to the potential risk of enhancing HIV-1 replication because of the release of tumor necrosis factor-α and/or the transient oxidative stress. On July 1995, we decided to investigate whether a well-standardized method of ozonated autohemotherapy (O_3-AHT) [5] could affect immunologic and virologic markers of the course of HIV-1 infection in drug-naive patients. This decision was taken because: first, some patients refused antiretroviral therapy; second, there was a considerable interest in using ozone therapy in HIV infection; and third, it could not be foreseen that the actual triple antiretroviral regimen would be so effective. The study population was limited initially to 10 HIV-1- and hepatitis C virus-positive adults enrolled in 1995–96, who signed an informed consent to be treated by ozone therapy. The treatment consisted of collecting 300 g of blood from each patient in a Baxter bag for autotransfusion (mod. RO530) and exposing it to 300 mL of 95% O_2/5% O_3 at an O_3 concentration of 67 mg/L (20.1 mg O_3 per treatment). Because of a low prothrombin time (PT), citrate–phosphate–dextrose–adenine (CPDA) was used as the anticoagulant for blood from patient 3263. Blood samples from all of the other patients were treated with heparin calcium salt (30 U/g blood) after CPDA had been eliminated from the bag. Blood was mixed thoroughly with the gas, avoiding foaming for at least 5 min until pO_2 reached a plateau at about 400 mmHg and ozone had fully reacted with blood. Immediate retransfusion

was completed in about 20 min. O_3-AHT was carried out twice weekly for at least 16 sessions. Measurements performed at weeks 1 and 8 with respect to the initiation of O_3-AHT included standard hematologic parameters, β_2-microglobulin level, $CD4^+$ T-lymphocyte count, HIV-1 p24 antigenemia, and HIV-1 cellular DNA and plasma RNA load as assessed by competitive PCR and RT-PCR procedures [6].

Three patients withdrew from the trial before completion for reasons unrelated to the procedure and were excluded from data analysis. Because of a marked sense of wellbeing, patients 6713, 2189 and 210 demanded further treatment and underwent 54 O_3-AHT sessions, receiving an overall ozone dose of 1080 mg evenly distributed in 16.2 L of blood. No patient reported any side effect, and hematologic parameters remained stable or improved. A few patients noted a decreased incidence of oral candidosis and herpes labialis. Table 1 shows the results of the 8-week O_3-AHT trial. With the exception of patient 3263, there was a significant increase in $CD4^+$ cell numbers ($p=0.001$ when patient 3263 is not included). Interestingly, patient 3263 received blood anticoagulated with CPDA because of a PT ranging between 62% and 69%. Use of heparin, by preserving the physiologic Ca^{2+} level in plasma, enhances immune activation [7]. $CD8^+$ T-lymphocyte counts remained practically stable. Plasma HIV-1 RNA and leukocyte HIV-1 DNA levels were not significantly affected by the treatment, suggesting that ozone does not express a direct virucidal effect in vivo. HIV-1 p24 antigenemia was and remained negative in all patients. Serum β_2-microglobulin increased significantly, possibly as a result of O_3-AHT-mediated immunologic enhancement [5]. Analysis of the three long-term ozone-treated patients at week 24 confirmed sustained CD4 counts and stable viral load (not shown).

While in the lay press there have been many undocumented claims that O_3-AHT is effective in HIV-1 infection, the possibility that a supplemental oxidative stress may accelerate disease progression by enhancing HIV-1 replication in vivo has not been tested before. Although the present study analyzed a limited number of patients, repeated measurement of relevant virologic markers indicated that ozone therapy carried out with an accurate and reliable method neither improves nor worsens the dynamics of HIV-1 replication. Ozone-mediated upregulation of HIV-1 replication could not have occurred, probably because the oxidative stress of O_3-AHT is extremely transient and actually enhances the expression of superoxide dismutase [8] which is normally suppressed by HIV-1 Tat protein [9].

Table 1 Evaluation of surrogate markers in HIV-1 infection before and after ozone therapy

Patient	Week	CD4/μL	β_2-Microglobulin (mg/L)	HIV-1 DNA (copies/10^6 CD4)	HIV-1 RNA (copies/mL)
6011	−1	255	3.1	42 462	317 857
	8	307	3.7	48 956	335 000
6713	−1	294	2.0	26 974	54 182
	8	404	3.6	36 343	26 049
6968	−1	222	2.7	36 545	169 043
	8	362	4.1	25 841	135 179
2189	−1	254	3.7	24 359	9 886
	8	368	5.5	41 612	17 190
210	−1	127	5.6	12 650	333 554
	8	179	6.0	6 327	934 619
3263	−1	298	3.1	168 047	33 812
	8	198	4.6	147 572	11 495
6679	−1	454	7.4	71 692	16 125
	8	571	6.5	97 341	23 229
Mean±SD	−1	272±99	3.9±1.9	54 681±53 340	133 494±141 750
	8	341±133	4.9±1.2	57 713±48 466	211 837±339 494
p		0.066	0.045	0.640	0.937

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