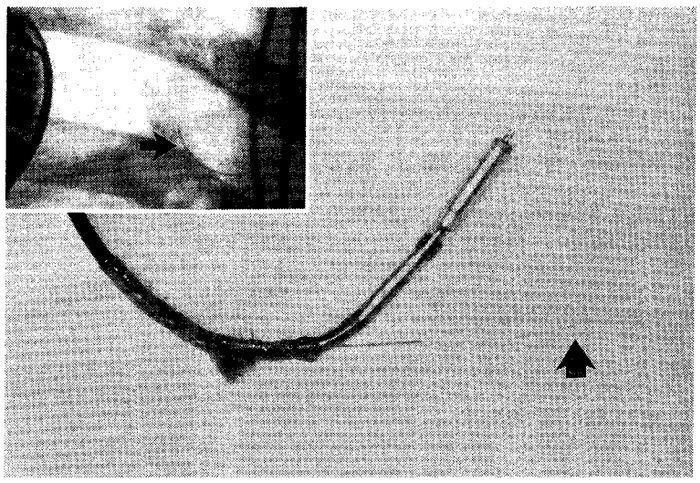

Figure: **Preoperative chest radiograph and removed electrode**
Arrows=free-floating wire and fracture.

329-701, and 033-812 electrodes. The chest radiograph revealed that the J-support wire had fractured and detached from the insulating sheath (figure). The patient was transferred to us.

Transthoracic echocardiography revealed no significant abnormality, but transoesophageal examination showed prolapse of the support wire. There was a large pedunculated mass attached near the base of the free-wall tricuspid valve-leaflet (not seen on transthoracic echocardiography). Clinically, there was no evidence of infective endocarditis. At median sternotomy, the pericardium adjacent to the right atrial free-wall was multiply perforated and the fractured atrial-J support wire protruded from adhesions between the right main pulmonary artery and the posterior wall of the ascending aorta. The wire was removed easily and cardiopulmonary bypass was established, followed by right atriotomy.

The insulation on the atrial electrode had degenerated for 5 cm from the proximal bipole and about 1·5 cm of rigid straight wire protruded from the atrial electrode and penetrated from the posterior aspect of the right atrium adjacent and perpendicular to the aortic root. The electrode tip was in the right atrial appendage and was easily unscrewed and removed with protection of the atrial myocardium from the free support-wire (figure). A 2×2 cm mass densely adherent to the right atrial wall and adjacent to the anterior tricuspid valve-leaflet was excised. A new dual-chamber pacing system was implanted. The patient made an uneventful postoperative recovery and was discharged on the seventh postoperative day with normal pacemaker function. The right atrial mass had extensive eosinophilic inflammation and dense fibrosis consistent with organised thrombus. Cultures were sterile.

More than 47 000 Telectronics Accufix atrial-pacemaker leads (models 330-801, 329-701, and 033-812) have been implanted world wide. After reports of electrode degeneration, the manufacturers recommended chest radiography ideally with fluoroscopy to look for defects (Telectronics Pacing Corporation, November, 1994). In addition, follow-up of 1000 patients has started in the USA with interim findings of a 12% frequency of suspected support-wire fracture and a 1·4% detection rate of support-wire protrusion in these cases by radiography (data from Telectronics). The report suggests that a bulge in the insulation proximal to the J curve may indicate imminent penetration of the support wire, although most fractured support-wires have not yet penetrated the outer insulation. Electrode motion on fluoroscopy may indicate support-wire fracture. The question remains whether abnormal appearance on fluoroscopy demands urgent or elective intervention, or indeed, with what intervals fluoroscopy should be repeated (the current recommendation is six-monthly).

There have been two deaths from the degenerated electrodes in the USA caused by laceration of the aorta, as well as two non-fatal episodes of pericardial tamponade treated surgically (data from Telectronics). Our case confirms that the electrode degeneration can be life-threatening. Multiple puncture sites in the pericardium might explain the recurrent pericarditis diagnosed eight months earlier. Electrode-induced trauma caused a large thrombus to form that was not seen on conventional chest radiography, fluoroscopy, or transthoracic echocardiography, but was demonstrated on transoesophageal electrocardiography. Endovascular removal of the electrode attempted without atriotomy might have caused embolisation of the adherent thrombus with serious consequences.

Our recommendation is that all potentially defective Accufix electrodes should be removed via the endovascular route as an elective procedure. Accufix electrodes are easy to remove by this route with immediate insertion of a different type of atrial electrode, which seems to be the least traumatic method of managing these patients.

We intend to do cineradiography on all our patients with this Accufix electrode, and send all removed electrodes for testing to the manufacturer. This will allow assessment of the sensitivity and specificity of fluoroscopy as a guide to further management.

We thank Dr Graham Jackson and Dr Cliff Bucknall for their advice and Miss Geraldine Daly for secretarial assistance.

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Treatment of HIV-associated Kaposi's sarcoma with paclitaxel

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We investigated whether paclitaxel was active in AIDS-associated Kaposi's sarcoma. We gave 135 mg/m² intravenously over 3 hours every 21 days. Follow-up is available on the first 20 patients, most of whom had advanced Kaposi's sarcoma and severe immunocompromise. Neutropenia was the most frequent dose-limiting toxic effect; novel toxic effects included late fevers, rash, and eosinophilia. Creatinine increased in 2 patients and 1 patient had cardiomyopathy. There were 13 partial responses (65%, 95% CI 41–85%). All 5 patients with pulmonary involvement responded. Paclitaxel appears to be active against Kaposi's sarcoma as a single agent. Further studies, including a randomised trial, are warranted.

Lancet 1995; **346:** 26–28

Paclitaxel (Taxol) is active against carcinomas of the ovary, breast, lung, and head and neck.[1-3] The drug induces irreversible polymerisation of microtubules; its cellular target is thus similar to that of vinca alkaloids, although the latter depolymerise microtubules. Vinca alkaloids have activity against Kaposi's sarcoma, which led us to consider paclitaxel for this condition. Further support for a trial came from the findings that paclitaxel inhibited the growth of spindle cells derived from Kaposi's sarcoma (MWS and RY) and that it had anti-angiogenesis activity in vitro (K Duncan and E Sausville, National Cancer Institute). We started a phase II trial of paclitaxel in patients with HIV-associated Kaposi's sarcoma in September, 1993.

Patients were required to have biopsy-proven Kaposi's sarcoma for which systemic therapy was indicated, only one previous chemotherapy regimen, and adequate performance status and organ function. Antiretroviral therapy was optional but could not be changed within 2 weeks of entry. Patients initially received 135 mg/m^2 paclitaxel (provided by the Cancer Treatment Evaluation Program, National Cancer Institute) as a 3 hour intravenous infusion every 21 days. The dose was increased by 20 mg/m^2 each cycle to a maximum of 175 mg/m^2 if the absolute granulocyte count remained above 10^9/L. Patients received premedication with 10 mg dexamethasone orally 14 and 7 hours before infusion, and with 300 mg cimetidine and 50 mg diphenhydramine intravenously immediately before paclitaxel infusion. For grade 4 haematological toxicity (grading defined in table), the dose was decreased by 25%. Colony-stimulating factors were not used. Responses were assessed with modification of the method of Krown et al,[4] which uses skin-lesion dimensions, palpable nodularity, lesion number, and radiographic assessment of visceral lesions. In patients with extensive cutaneous disease, representative areas of the body were assessed.[4] Partial responses required a 50% diminution of at least one of these variables; complete responses required clinical and pathological resolution of all disease. Patients were considered evaluable after two cycles. Treatment was continued two cycles beyond best response or until progression. We report on the first 20 patients, up to Jan 25, 1995, which is 18 weeks after the 20th patient was entered (this was a data-collection cut off; the target sample size was 29). All patients were evaluable.

All patients were male, with a mean age of 38 (range 26–55). 16 had advanced, poor prognosis Kaposi's sarcoma;[4] 5 had pulmonary disease, a life-threatening manifestation. Most patients were severely immunocompromised (median CD4 count at entry 16/μL, 0–318). Only 4 patients had greater than 50 CD4 cells per μL. 6 had known active opportunistic infections, including 3 with *Mycobacterium avium* complex bacteraemia, 2 with presumptive cerebral toxoplasmosis, and 1 with microsporidia colitis. 16 were taking antiretroviral therapy.

13 patients had a partial response (65%, 95% CI 41–85%). No patient achieved complete response, 6 were stable, and 1 progressed. All 6 patients who had received previous systemic treatment responded, as did all 5 with pulmonary Kaposi's sarcoma (figure). The median time to achieve response was 17 weeks (range 9–36), with a median of six cycles of therapy per patient (two to over nineteen). Median Kaplan-Meier progression-free survival among the partial responders was 34 weeks (15-60+). Median time to progression after discontinuation of therapy was 10 weeks (8–18). 12 patients required dose reduction below 135 mg/m^2, and the average received-dose intensity, calculated over the first nine cycles of therapy (100% intensity=56 mg/m^2 per week)[5] was 38·8 mg/m^2 per week (69%).

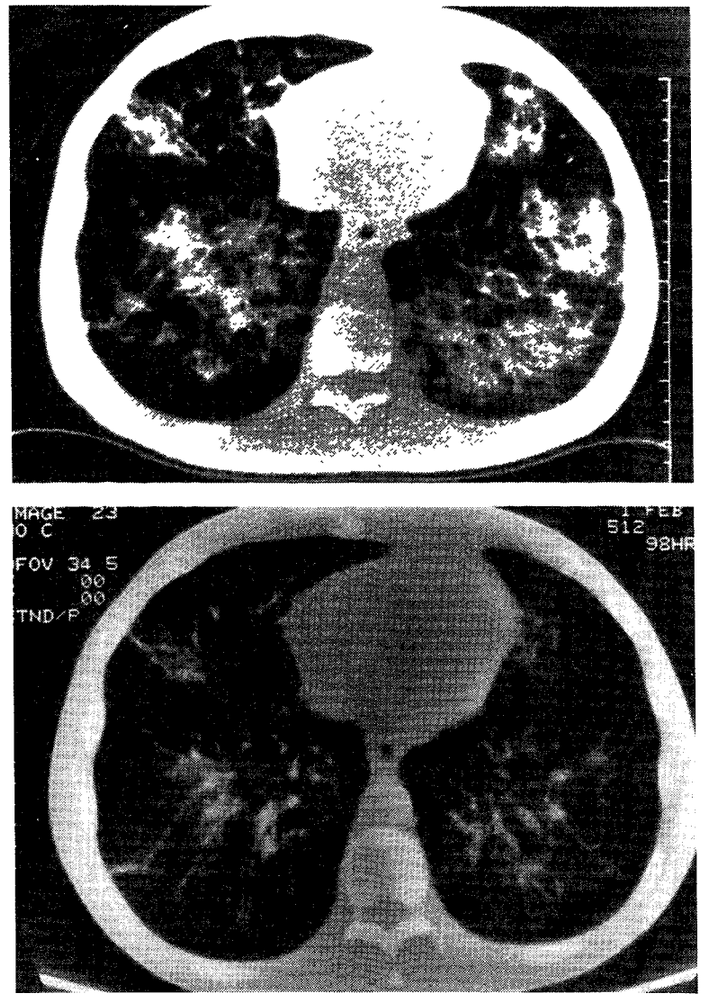

Figure: **Computed tomography of patient with pulmonary Kaposi's sarcoma**

Upper scan shows characteristic infiltrative/micronodular appearance of Kaposi's sarcoma lesions in lung. Lower scan followed two cycles of paclitaxel and shows improvement.

Toxic effects were, in general, similar to those seen with paclitaxel in other settings (table). The most frequent dose-limiting toxic effect was neutropenia, which usually resolved before the next cycle of therapy was due to start. Several possibly novel toxic effects of paclitaxel were seen, including delayed rash, renal failure, cardiomyopathy, delayed fevers, and eosinophilia. An urticarial rash was observed in 5 patients 7–10 days after one course of paclitaxel. 2 African-American patients developed acute renal failure, 1 with accompanying cardiomyopathy. Whilst these are known complications of HIV infection,[6] a

Toxic effect	Grade 3	Grade 4
Clinical		
Delayed fever	2	0
Diarrhoea	1	0
Cardiomyopathy	0	1
Laboratory		
Neutropenia†	3	14
Anaemia	6	0
Thrombocytopenia	2	0
Renal failure (increased creatinine)	1	1
Hyperglycaemia	5	0
Hyperamylassaemia	1	0
Increased hepatic enzymes	0	1

*As defined by Common Toxicity Criteria, Clinical Trials Evaluation Program, National Cancer Institute. Toxic effects are listed if they were possibly or probably related to paclitaxel administration. †1 episode of sepsis (without documented bacteraemia) occurred.

Table: **Severe toxic effects***

relation with paclitaxel administration could not be ruled out. 2 other patients developed temperatures to 40°C without evidence of infection 18–20 days after paclitaxel administration for up to four consecutive cycles. 1 patient also had activation of previously quiescent psoriasis. Finally, eosinophilia (defined as a three-fold increase) occurred in 40% of patients; it was not associated with increased plasma concentrations of interleukin-4, interleukin-5, or granulocyte-macrophage colony-stimulating factor. Other toxic effects associated with paclitaxel were generally mild and often difficult to distinguish from the underlying disease. 4 patients died during the study: 1 from hepatic failure associated with chronic active hepatitis B and recent initiation of total parenteral nutrition; 1 after treatment for central-nervous-system lymphoma and *Pneumocystis carinii* pneumonia; 1 from progressive pulmonary infiltrates of unknown cause; and 1 from thrombotic thrombocytopenic purpura (the patient with cardiomyopathy). 5 other patients have died of AIDS-related causes after completion of the study, which gives an overall median Kaplan-Meier survival of 13 months.

One concern about the use of myelosuppressive agents in AIDS is their potential for inducing further immunosuppression. In the patients who completed four cycles of therapy, median CD4 count fell from 14 to 5 per μL (median change −5, interquartile range −11 to 0). 8 patients developed a total of 11 opportunistic infections, including 4 episodes of cytomegalovirus disease, while in the study. This gives an incidence of 1 opportunistic infection for every 11·8 person-months, which is within the expected rate for this population.[7,8] Also, 2 patients developed non-Hodgkin lymphoma (1 may have had pre-existing disease). Median serum p24 antigen was stable (median change 0 pg/mL, 0 to 36).

Overall, these results compare favourably with those of other single agents or combination regimens for Kaposi's sarcoma.[9] Our results suggest that paclitaxel has activity in patients with HIV-associated Kaposi's sarcoma, including those with aggressive disease, advanced AIDS, or previous receipt of systemic therapy. Complete responses are rare in such a population and although our partial response rate was high, a randomised trial would be required for comparison with other regimens. The toxicity profile was similar to that previously reported for paclitaxel. However, certain novel toxic effects were observed, and doctors prescribing this drug in HIV-infected patients should be alerted to the possibility of yet other unexpected toxic effects.

The responses we report were obtained without the use of bone-marrow-stimulating cytokines. A better response rate might be obtained with use of granulocyte colony-stimulating factor and higher doses of paclitaxel. However, any potential palliative benefits would need to be weighed against the added treatment complexity and increased cost. Also, the 3 hour infusion schedule was used largely because of its convenience of administration, but better response rates or less toxicity may be attainable with a longer infusion duration (MWS, WHW, RY).

We thank Bristol-Myers Squibb for financial support. We also thank the medical and nursing staff of the NIH Clinical Center and the Medicine Branch of the NCI; Dr B Goldspiel and Dr D Kohler of the Clinical Center pharmacy service; Dr R E Wittes, Dr S Arbuck, Ms K Wyvill, Ms L Shay, and Dr E Reed of the NCI, Dr J A Bailey of St Vincent's Medical Center, New York; and Dr R Cohen of the University of Virginia Cancer Center, Charlottesville.

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