Short-Course Chemotherapy for Tuberculosis with Largely Twice Weekly Isoniazid-Rifampin

To the Editor:

The article on short-term chemotherapy by Dutt, Jones and Stead and the accompanying editorial by Lester was very welcome and important. Together with many other studies it emphasizes the need for a long overdue policy decision in the United States in favor of using short-term chemotherapy regimens for treating tuberculosis.

Of particular interest in the study by Dutt et al was the use of intermittent isoniazid and rifampin. Such intermittent programs are extremely useful in treating patients judged to be unreliable, because they make it feasible to have a member of the health department observe the ingestion of each dose of medication. However, because of the potential for serious hypersensitivity reactions, especially severe thrombocytopenia when rifampin is given intermittently, the regimen described by the authors, self-administered, twice-weekly isoniazid and rifampin appear unnecessarily dangerous. Fortunately, the superficial surveillance program employed, namely periodic checkups by public health nurses and instruction of the patient to check for "red spots" before taking each dose, prevented serious toxicity, such as a stroke, from occurring in their one patient with thrombocytopenia. However, if a larger number of patients were treated, a few cases of serious toxicity would be likely to occur. A much safer and generally accepted way to use rifampin intermittently is to have health department personnel fully supervise each dose to ensure its ingestion and to permit questioning of the patient concerning hypersensitivity symptoms, especially purpura, before the next dose is given.

If self-administered short-term regimens containing rifampin are to be used, it is probably safer to give rifampin daily to reduce the chance of serious hypersensitivity reactions. The increased per-patient cost of daily isoniazid and rifampin for nine months ($226.00) compared to $78.00 for the largely intermittent isoniazid and rifampin used in the study is an expense that most health departments in the United States can and should pay. In addition, daily medica-

tion is probably more likely to succeed in converting sputum cultures to negative and maintaining culture-negative status, as demonstrated by close to 100 percent success with the daily regimen of isoniazid and rifampin for nine months and only 96.7 percent success for the largely intermittent regimen reported by Dutt et al.

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REFERENCES


To the Editor:

Dr. Moulding raises the question of the propriety of using twice-weekly medication in this country except where direct supervision of the ingestion of each dose is necessary to assure compliance. When we began to treat older patients with largely self-administered twice-weekly medication, the possibility of serious allergic reactions to rifampin (RIF) was of concern to us, particularly thrombocytopenia. However, most serious reactions to RIF were reported to occur when a dose of 1200 mg was used or the drug was given at weekly intervals. Now, after having treated over 600 patients using 600 mg of RIF twice a week, we feel quite reassured. We have encountered only three instances of petechial hemorrhages and only one of these was accompanied by thrombocytopenia. Real danger can usually be averted if the patient and/or a responsible person caring for the patient is acquainted in advance with the need to be alert for early signs of bleeding, such as petechiae or purpura of the legs. This is not to say that when much larger numbers of patients are treated in this fashion throughout the country there will not be instances of purpura, renal impairment, flu-like syndrome, etc. It is only to say that the risks are not great and that if care is taken, the risks are out-weighed by the advantages of the simplified regimen. Moreover, Dr. Moulding’s objection loses some force when one considers that there are reports in the literature of thrombocytopenia developing in patients receiving well supervised daily RIF.

Dr. Moulding seems to draw a distinction between “close to 100 percent success for daily administration” and the “96.7 percent success” that he attributes to our largely twice-weekly regimen. (The figure we gave was 95 percent but Dr. Moulding appears to have recalculated it.) When one considers that we reported on all our failures and did not exclude uncooperative patients or early deaths from analysis, we submit that 95 percent is better than can usually be achieved with any other regimen.

Dr. Moulding seems also to have missed some recent developments in fiscal matters. Despite the great influence of the US, health department budgets are being cut seriously throughout this country. Funds are not available to permit waste of money. The difference in $78 for drugs on our regimen and $226 for daily administration cannot be viewed as insignificant. We admit the results of daily administration
are as good as ours, but know of no evidence that they are better. So why use more medicine than is necessary?

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REFERENCES
2 Hong Kong Tuberculosis Treatment Services/Brompton Hospital/British MRC: A Controlled trial of daily and intermittent rifampicin plus ethambutol in the treatment of patients with pulmonary tuberculosis: results up to 30 months. Tubercle 56:179, 1975

Acute Upper Airway Obstruction

Sodium Warfarin-induced Hemorrhage into the Base of the Tongue and Epiglottis

To the Editor:

The location and clinical features of anticoagulant-induced bleeding are quite variable. Fortunately, such bleeding into the upper respiratory tract with subsequent upper airway obstruction is rare. Retropharyngeal hemorrhage and associated airway obstruction due to sodium warfarin have been described.1,2 We report the first case of upper airway obstruction from spontaneous hemorrhage into the base of the tongue and epiglottis secondary to sodium warfarin administration.

CASE REPORT

A 41-year-old woman was admitted to the respiratory intensive care unit of Mount Sinai Services-City Hospital Center at Elmhurst with partial upper airway obstruction. Four days prior to admission she had had a mild upper respiratory tract infection. On the morning of admission she developed a sore throat and dysphagia after a vigorous coughing episode. She noticed swelling of her neck and inability to lie down due to respiratory difficulty. She had been taking digitalis, diuretics, and sodium warfarin 5 to 10 mg daily for the last nine years since mitral valve replacement for rheumatic mitral stenosis. A cardiac catheterization study one year previously revealed moderately severe pulmonary hypertension, severe tricuspid insufficiency, biventricular failure, and a normally functioning mitral valve prosthesis. There was no history of recent trauma to the neck.

On physical examination she was sitting anxiously in bed. Vital signs were within normal limits. Examination of the oral cavity revealed a submucosal hematoma at the base of the tongue, vallecula, epiglottis, and right parapharyngeal wall. The right side of her neck below the mandible was swollen and slightly tender. There was mild neck vein distention. In the supine position, inspiratory stridor was heard over the neck. Examination of the heart revealed a pansystolic grade 2/6 murmur at the lower left sternal border and a normal prosthetic click. There was a trace of ankle edema. The remainder of the physical examination was normal.

A lateral soft tissue x-ray film of the neck showed swelling of the base of the tongue and epiglottis with obstruction at the junction of the epiglottis and posterior pharyngeal wall (Fig 1). Chest x-ray examination showed cardiomegaly with a prosthetic mitral valve. The partial thromboplastin time was 144 seconds (control 35 sec) and prothrombin time, 60 sec (control 12 sec). Arterial blood gas levels showed no hypoxemia and mild respiratory alkalosis. Our impression was that she had partial upper airway obstruction especially in supine position, and she did not require immediate intubation or tracheostomy because she had adequate alveolar ventilation. She was given two units of fresh frozen plasma, 10 mg phytonadione subcutaneously, and cough suppressants. Within 24 hours, the abnormal coagulation times returned to normal and the submucosal hematoma began to resolve. She was able to lie down and swallow liquids. A repeat lateral soft tissue x-ray film of the neck six days later showed almost complete restoration of the upper airway. Follow-up oral examination revealed mild ecchymosis over the base of the tongue and epiglottis. She continued to improve, was restarted on warfarin, and discharged on the 13th hospital day.

DISCUSSION

This patient developed hemorrhage into the base of the tongue and epiglottis and partial upper airway obstruction while on sodium warfarin. Several factors may have contributed to the occurrence of hemorrhage: the presence of venous congestion due to upper respiratory tract infection and right-sided heart failure, a forceful coughing episode which may have ruptured small blood vessels, and, most significantly, a markedly prolonged coagulation time due to sodium warfarin. Lepore3 described a case of sodium warfarin-induced bleeding into the floor of the mouth which involved the sublingual and submaxillary spaces, pushed the tongue upward and backward, and led to upper airway obstruction.

Anticoagulant-induced bleeding into the retropharyngeal area,1,3 sublingual space,4 or base of the tongue and epiglottis as in this report can all lead to upper airway obstruction. This life-threatening condition, when promptly recognized, can be treated successfully with discontinuation of anticoagulants, administration of fresh frozen plasma and vitamin K, close airway monitoring, and immediate intubation or tracheostomy if necessary.

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