plain the sleepiness, since about one-third of all patients with hypersomnia and sleep-induced apnea are not significantly obese. The hypoxia found in this group is of special interest, since we have suggested that hypoxic alterations of brain-stem biogenic amine synthesis and metabolism due to a selective sensitivity of catecholamine and serotonin enzymes may take place in man, as they do in rats, and might contribute to sleepiness in the daytime. It does not seem likely the sleepiness is directly caused by the disorder of the central nervous system that is presumed to be responsible for sleep-induced apnea, since sleepiness is one of the symptoms that is promptly reversed by tracheostomy.

This important, complex clinical syndrome provides an exciting interface among the fields of sleep disorders, neurology, cardiology, and pulmonary medicine. There are many unanswered questions concerning the syndrome of hypersomnia and sleep-induced apnea. How many cases of sudden unexplained death during sleep in obese middle-aged individuals are due to this hidden illness? What is the relationship among “central alveolar hypoventilation,” the pickwickian syndrome, and the syndrome of hypersomnia and sleep-induced apnea? Clarification of the differential diagnosis and the establishment of a nosology of these disorders is critical if we are to properly evaluate drugs such as progesterone, amitriptyline, imipramine, amine, and others that are presently used on an ad hoc basis in individual cases. New effective quantitative methods are needed to measure the sequential night-by-night type, frequency, and severity (eg, degree of hypoxia) of apnic episodes at home. Is loss of weight an effective long-term treatment in obese patients with the syndrome of hypersomnia and sleep-induced apnea? What is the age and sex prevalence of “benign” snoring, compared with “malignant” snoring with apnea, in the general population? How many hypertensive middle-aged men and women have sleep induced apnea? What is the prevalence of sleep-induced apnea in the middle-aged obese, and how much does it contribute to the increased risk of morbidity and mortality in these individuals? Why is there such a significant sex difference (figures range from 10:1 to 25:1 in favor of men)? What is the familial incidence of the syndrome of hypersomnia and sleep-induced apnea and the relationship of this syndrome to the sudden infant death syndrome? Is there a selective risk of hypoventilation and apnea during sleep in patients with other forms of pulmonary disease, especially chronic obstructive pulmonary disease?

These questions and others pose a major challenge and should attract talented clinical and basic scientific investigators. The policies and availability of research and postgraduate financial support through governmental and private funding agencies will therefore have a direct impact on the lives of many patients who have the syndrome of hypersomnia and sleep-induced apnea and who have related sleep disorders.

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Short-Course Chemotherapy for Tuberculosis

The search for the ideal regimen of antituberculosis chemotherapy continues. Such a regimen would be one of maximum efficacy with minimum cost, duration, and toxic effects and, thus, most acceptable to patients. Therefore, the article by Dutt, Jones, and Stead in this issue (see page 441) reporting the results of the Arkansas program of short-course chemotherapy is of great relevance and interest. These investigators provide significant evidence regarding the efficacy of such a program based upon the daily administration of isoniazid and rifampin for 30 days, followed by twice-weekly administration of these drugs for eight months. In

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addition, the results indicate that utilizing their schedule of dosage, the overall incidence of toxic effects was remarkably low and certainly in the acceptable range.

There are two factors in the Arkansas study which warrant further discussion. One is the extent to which the patients were checked, both for compliance in terms of the ingestion of drugs and for adverse reactions. The second factor is the fact that the dosage of rifampin during the twice-weekly phase was 600 mg, rather than the 900 to 1,200 mg used in other studies.

To those with experience in traditional long-term antituberculosis treatment, it seems miraculous that a regimen requiring less than 100 doses of medicine over a nine-month period would be so effective as to be competitive with any other therapeutic program; however, the Arkansas study certainly suggests that this is the case. Moreover, with such a schedule, it is obvious that any failure in the patient's compliance becomes highly significant. One important factor in the Arkansas study was the intensity with which the ingestion of the drugs was monitored. This point should be emphasized so that the design of any future short-course program should include the provision of adequate facilities to monitor patients and, when indicated, directly supervise the ingestion of drugs. Thus, some of the anticipated savings from the short-course program should be reinvested in quality control, and the overall results will be greatly improved.

The second factor of interest in the Arkansas study is the relatively low rate of adverse reactions encountered during the twice-weekly phase. Studies performed overseas, using rifampin in a twice-weekly dose of 900 to 1,200 mg, revealed a significant frequency of hypersensitivity reactions to rifampin, supported by the demonstration of antibodies to the drug. On the other hand, daily administration at a 600-mg dosage failed to produce this hypersensitization. These findings clearly inhibited the use of rifampin in a high-dose twice-weekly regimen. In the Arkansas study, rifampin was given in a dosage of 800 mg, and hypersensitivity reactions occurred in only three out of 288 patients. In addition, at this dose the Arkansas investigators were unable to demonstrate antibodies to rifampin in the serum of their patients.

In conclusion, it is hoped that the promising results of this Arkansas study in terms of maximal efficacy and minimal toxicity will encourage further careful evaluations of short-course regimens of antituberculosis chemotherapy. It seems quite clear that given adequate administrative and clinical support, such programs will greatly serve to extend the revolution in chemotherapy for tuberculosis, which began only 30 years ago.

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Grain Dust and Health

It has been known for centuries that grain dust can cause acute conjunctival, nasal and respiratory symptoms in susceptible individuals. The consequences of symptomatic, recurrent, long-term exposure, however, have not been established with certainty. Epidemiologic studies have shown that 40-75 percent of grain workers experience symptoms of cough, expectoration, wheezing, chest tightness, eye and nasal irritation when exposed to high concentrations of grain dust. Six to 33 percent have experienced one or more episodes of "grain fever," which occurred during exposure or several hours later. About one-third of the workers also suffered from chronic bronchitis and have evidence of abnormal airways flow at low lung volumes. Although it is clear in all reports to date that cigarette smoking is the predominant host factor in grain workers with chronic obstructive pulmonary disease, more current information by Dosman, Broder, and doPico (unpublished information) suggests that the effects of dust and smoking are additive, if not synergistic.

The acute and chronic effects of inhalation of grain dust are largely on the airways and not in the parenchyma as judged by the absence of radiographic changes and/or absence of abnormalities in pulmonary diffusing capacity.

Whether the mechanisms by which grain dust induces acute and/or chronic respiratory mucosa reaction are allergic, mechanical or chemical is not yet clear. It is possible that all three mechanisms are responsible. Warren and co-workers reported immediate and late asthmatic reactions to grain dust compatible with a hypersensitivity reaction to grain dust. In this issue of Chest (see page 461), Chan-