

comparable to that of morphine, and he concluded that increased misuse of oxycodone-containing drugs had caused the addiction of numerous persons not associated with the illicit drug trade. Since then the oxycodone-containing drugs (eg, Percodan) have been reclassified under the narcotic control laws. In view of the essentially equal analgesic and single-dose side effects when compared to codeine, there would seem to be little reason for the physician to subject his patient to the increased addiction hazard of the oxycodone analogue.

Another major difference between these three effective analgesic combinations is cost. On the basis of the average cost among a hospital pharmacy, a medical-center pharmacy, a chain-store pharmacy, and a privately owned neighborhood pharmacy in Rochester, Minn, on July 11, 1973, one hundred doses of oxycodone (9.76 mg) plus aspirin (200 Percodan tablets) will cost the patient \$18.12. One hundred doses of codeine sulfate (65 mg) plus aspirin will cost \$10.61. Pentazocine is not marketed in combination with aspirin, and to obtain the combination tested in this study, the patient must break a 50-mg pentazocine (Talwin) hydrochloride tablet in half and take aspirin separately. It would seem worth the nuisance, however, since 100 doses of 25 mg of pentazocine hydrochloride (50 Talwin hydrochloride tablets) cost only \$4.95.

Study Methodology: Strengths and Limitations.—The methodology of this study was purposefully designed to approximate closely the conditions that exist when the physician prescribes an analgesic for an ambulatory patient with a pain problem. The

patient went about his usual life activities during this study, and the patient himself selected the time when he felt an analgesic was required. By this means, the therapeutic procedure was tested in the same setting in which it would be applied clinically. Also, the subjective result was recorded directly by the patient without the possible distortion that could be introduced by a physician, nurse, or technician interviewer. Although this method has obvious advantages, it also has some very definite limitations. Accuracy of results is dependent on the reliability of the patient in following instructions and upon his ability to record observations clearly.

Innumerable uncontrolled variables may and frequently do influence the patient's response to each of the individual drugs studied. These include changes in his emotional status, whether he is rested or fatigued, the many and varied environmental stresses to which he may be subjected, whether the drug is taken in a fasting state or on a full stomach, whether the patient is active or at rest after taking the medication, and others. If, however, the experimental system is sensitive and of rational design, these uncontrolled variables should distribute themselves with reasonable uniformity throughout the population studied, so that statistical analysis will recognize differences in therapeutic effect if they exist. In this study, there were built-in quality controls of sensitivity provided by known differences between the drug preparations that should be detectable. Aspirin has an analgesic activity established by numerous investigators, and in this study aspirin was significantly

superior to placebo by all means of statistical analysis. In addition, both pentobarbital and promazine have a well-established sedative activity, and in this study both showed a statistically significant increase in sedative activity in comparison to placebo. On the basis of this evidence, we feel justified in presuming that our study design is adequate to detect both analgesic activity and side effects under conditions closely simulating the circumstance when an oral analgesic preparation is prescribed in clinical practice. We must emphasize, however, that our results can be strictly applied only to the patient population and methods we employed. They cannot be interpreted as representative of the analgesic response that may be obtained for pain problems of different etiology, nor can they be assumed to have any direct application to the long-term response to analgesic agents.

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