relief—1.2 hours. The median duration of analgesia ranged between four and six hours except for the more ineffective placebo, ethoheptazine and propoxyphene, which had median durations of analgesia of three to 3.5 hours.

At the dosages employed, most agents studied produced no more side effects than placebo. Pentazocine, however, resulted in a greater frequency of gastrointestinal and central-nervous-system side effects than all other agents tested, and one patient suffered a severe mental aberration with hallucinations after treatment with this drug.

Of special interest was the response of these patients with cancer pain to placebo: 21 per cent claimed greater than 50 per cent relief of pain with a dummy medication (Fig. 1). Placebo therapeutic and side effects seemed to be characteristic responses of particular patients, extending to their response to active drugs. The overall analgesic effect of active agents in the patients who responded to the placebo was a mean relief of 54 per cent as compared to only 39 per cent in those who did not respond (p less than 0.01). Similarly, patients who experienced side effects to placebo had more than twice the frequency of side effects to active agents (56 vs. 22 per cent). Patients who experienced a placebo analgesic effect were also more characteristically those who would experience placebo side effects.

DISCUSSION

In this study, simple aspirin at a dosage of 650 mg (10 gr) was the superior agent for relief of cancer pain among the tested marketed analgesics. Indeed, among all analgesics and narcotics available for oral use, none have been demonstrated to show a consistent advantage over aspirin for the relief of any type of pain. Beaver (3) has collected 36 controlled studies from the literature also showing aspirin to have a significant advantage over placebo for relief of pain from a variety of etiologies. Although gastrointestinal bleeding and allergic reactions undoubtedly occur as side effects of aspirin ingestion, the rate of these complications in clinically important form must be very low in view of the many tons of aspirin consumed collectively each year by nearly every adult and child in this country. These advantages, coupled with minimum price (usually less than $1 for 100 doses of 650 mg), should make the aspirin the drug of preference for any pain problem requiring an oral analgesic. It has been our own experience that if aspirin is recommended with the strong endorsement of the physician, it is acceptable to even the most sophisticated patient.

The para-aminophenol derivatives, acetaminophen and phenacetin, also showed superiority to placebo in this study; although they ranked lower than aspirin by all means of analysis, this difference was not statistically significant. Side effects of these agents are primarily problems of drug abuse and not of usual therapeutic doses. When they are prescribed generically, their price is only moderately higher than that of aspirin (in the range of $2 to $3 per 100 doses of 650 mg), and they seem to be a reasonable alternative of therapy in cases of aspirin intolerance.

Mefenamic acid (Ponstel), pentazocine (Talwin) and codeine all gave evidence of real analgesic effect. Both mefenamic acid and codeine, however, may produce troublesome gastrointestinal side effects with chronic use, and pentazocine may induce sedation, dizziness, impaired thinking or even hallucinations, so that the patient should be warned not to engage in any activity in which his impaired performance could result in danger to himself or others. Particularly troublesome are the price tags on these agents; mefenamic acid, $9.72 per 100 doses of 250 mg; pentazocine, $9.88 per 100 doses of 50 mg; and codeine, $12.08 per 100 doses of 650 mg.*

The therapeutic credentials of both propoxyphene (Darvon, $9.50 per 100 doses of 65 mg)* and ethoheptazine (Zactane, $7.40 per 100 doses of 75 mg)* must be classified as very equivocal. In this study, neither showed a significant advantage over placebo, and both were significantly inferior to aspirin. The dubious record of propoxyphene in controlled clinical trials has recently been reviewed by Miller et al. (4) This is the eighth published study in which propoxyphene has not shown any significant superiority over placebo. The qualifications of ethoheptazine seem even more questionable. Of five controlled studies now published, (5–8) only one (5) showed ethoheptazine to have any indication of analgesic activity.

Promazine was chosen for this study because it was one of the few phenothiazines to show analgesic activity in the study of Dundee and Moore (9) published

*Average price at a hospital pharmacy, a medical-center pharmacy, a chain-store pharmacy and a privately owned neighborhood pharmacy, Rochester, Minn., January 1, 1971.