

TABLE V.—UNDESIRABLE SIGNS AND SYMPTOMS

[Percentages represent patients (out of 60 placebo treated and 53 drug treated) who reported an occurrence on 1 or more visits after therapy started]

Sign or symptom	Frequency (percent)	
	Placebo	Drug
Pruritus.....	38	58
Skin rash.....	32	53
Headache.....	48	53
Abdominal pain.....	47	49
Tinnitus.....	37	47
Nausea.....	38	45
Dizziness.....	35	43
Blurred vision.....	20	43
Diarrhea.....	20	40
Anorexia.....	30	38
Stomatitis or sore tongue.....	15	30
Vomiting.....	15	23
Photophobia.....	10	13
Miscellaneous.....	63	75

Variables other than therapy—The samples were too small to provide sensitive tests of the relationship between the outcome of the trial and such variables as age, sex, duration of disease at start of trial, presence or absence of rheumatoid factor and differences between clinics. The data did not, however, suggest any close relationship between these variables and the improvement rates or drug-placebo differences.

CONCLUSIONS REGARDING DRUG EFFECTS

Three overall measures (functional class, observers' assessment and the five point scores) have shown differences in percentage frequency of improvement that were associated with the drug; and so also have certain individual indexes in patients who were severely affected at the beginning of the trial. "Association," however, does not imply causal relationship in a trial that cannot be maintained completely double-blind. It is conceivable that observers, nurses or others might have guessed at the patients' therapy from side-effects and then, probably unconsciously, they might have affected the patients' responses to questions and tests. To detect such an influence, the number of undesirable signs and symptoms reported on the final visit were compared with the observers' overall assessments and with the five point scores. No consistent relationship was found. Perhaps the test was too insensitive; but the magnitude of the percentage frequency differences in Table IV, taken along with other workers' experience with antimalarials, leaves little doubt that the drug-placebo differences were largely cause-and-effect relationships.

One must, of course, beware of accepting percentage differences found in samples of 50 or 60 patients as equivalent to what would be found in a study of much larger numbers of patients of the same kind and under the same conditions. The observers' figures for improvement were placebo—35 per cent, and drug—64 per cent, a difference of 29 per cent. Even if the patients in the trial were strictly random samples of their respective (placebo and drug) populations, all that the 29 percent could tell us would be that the true (population) difference was probably somewhere between 15 and 40 per cent.

SEROLOGICAL STUDIES

Sera collected from all patients at the beginning and end of the trial were sent to the Rackham Arthritis Research Unit in Ann Arbor, Michigan, for serological, chemical and electrophoretic studies. Complete pairs of sera were available from 50 drug- and 52 placebo-treated patients. We are grateful to Drs. George R. Thompson and Ivan F Duff for permitting us to summarize some of their results here prior to their own publication.

Latex agglutination tube test—Thirty-six drug- and 44 placebo-treated patients had positive tests initially. In 7 drug and 2 placebo-treated patients the tests became negative. When changes in titer of more than one tube up or down were examined, the following contrasts were observed: in the 50 drug-treated patients, a fall in 10 and a rise in 3; and in the 52 placebo patients, a fall in 5 and a rise in 6. Although these differences could have been accounted for by individual variation, it should be noted that they are in agreement with results