

A placebo-controlled multicenter study of auranofin in the treatment of patients with corticosteroid-dependent asthma

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Background: Previous clinical studies have demonstrated that injectable gold salts and the oral gold compound, auranofin, possess significant steroid-sparing effects in the treatment of asthma.

Objectives: The objectives of this investigation were to determine whether auranofin could reduce oral corticosteroid requirements and to evaluate the safety of auranofin in the treatment of chronic corticosteroid-dependent asthma.

Methods: Patients with asthma were eligible if they required at least 10 mg of prednisone per day for control and prevention of asthma exacerbations. Two hundred seventy-nine patients with chronic corticosteroid-dependent asthma (requiring ≥ 10 mg/day) were randomized to receive auranofin, 3 mg twice daily, or placebo during an 8-month clinical trial, which was divided into three phases including: a 4-week baseline period (phase I), a 6-month double-blind treatment and steroid reduction period (phase II), and a 4-week posttreatment observation period during which steroid and auranofin doses or placebo doses were maintained at levels achieved by the end of phase II (phase III). The primary efficacy variable was "therapeutic success" or reduction of daily corticosteroid use by 50% or more.

Results: The proportion of patients in the auranofin group achieving therapeutic success (41%) was significantly higher than that in the placebo group (27%) ($p = 0.01$). This effect was greatest in patients requiring 10 to 19 mg of oral prednisone per day at baseline ($p < 0.001$). In all treated patients, including those who did and did not complete the trial, significant reduction ($\geq 50\%$ of baseline) in oral corticosteroid dosage was achieved in the auranofin group (60%) compared with the placebo group (32%) ($p < 0.001$). There were no significant differences between treatment groups in symptoms, concomitant medication use, or lung function. Mean serum total IgE levels decreased significantly from baseline in the auranofin group (-44.63 IU/ml) compared with the placebo group ($p = 0.001$).

Gastrointestinal and cutaneous adverse events were greater in the auranofin group.

Conclusions: Auranofin demonstrated a steroid-sparing effect without concomitant worsening of symptoms or lung function and appeared to be more effective in patients dependent on 10 to 19 mg of prednisone per day. Therefore this study has demonstrated that auranofin is useful as a steroid-sparing agent in the treatment of chronic corticosteroid-dependent asthma. (*J Allergy Clin Immunol* 1996;98:317-24.)

Key words: Auranofin, oral gold, steroid-dependent asthma, steroid-sparing, antiinflammatory effects of auranofin

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Corticosteroids are the most effective agents for controlling airway inflammation in patients with asthma.¹ For this reason inhaled corticosteroids, which have minimal systemic adverse effects, have been recommended for the treatment of chronic asthma. However, a subset of patients with asthma becomes "steroid dependent" and ultimately requires daily maintenance doses of systemic corticosteroids despite treatment with maximal doses of inhaled corticosteroids. Because of adverse consequences and disabling side effects associated with these drugs, a number of "steroid-sparing agents" have been examined for their ability to reduce oral corticosteroid requirements in patients with severe asthma.²⁻⁴

Gold compounds are one group of agents that have been evaluated for steroid-sparing effects in asthma. Muranaka et al.^{5,6} reported that decreased symptoms, reduction of mean daily dose of oral corticosteroids, and improvement of nonspecific bronchial hyperresponsiveness could be achieved in such patients by administration of a parenteral gold salt, gold sodium thiomalate. Because auranofin, an oral gold compound, had a number of immunomodulatory properties, which could be particularly beneficial in the treatment of asthma,⁷⁻¹² an open pilot study was conducted in 20 patients with severe steroid-dependent asthma who received auranofin at a dose of 3 mg twice daily for 20 weeks in 1988.¹³

In a subsequent double-blind, placebo-controlled investigation of 32 patients with steroid-dependent asthma, Nierop et al.¹⁴ reported a significant reduction in mean maintenance steroid dosages in patients treated with auranofin compared with those treated with placebo (4 mg vs 0.3 mg) after 24 weeks of therapy. The results of these early studies suggested that auranofin is an effective adjunctive agent in the treatment of steroid-dependent asthma and provided the impetus for a much larger multicenter, placebo-controlled clinical trial of auranofin in the treatment of steroid-dependent asthma. The objectives of this clinical trial were to determine whether auranofin would facilitate reduction in oral corticosteroid dosages in patients with steroid-dependent asthma and whether its safety profile was acceptable in this subset of patients.

METHODS

Patient selection

Patient eligibility was determined by the following inclusion criteria: (1) a diagnosis of asthma as defined by the American Thoracic Society¹⁵ and a 15% increase in

FEV₁ after treatment with an inhaled β_2 -agonist, (2) a history of perennial asthma with symptoms of equivalent severity throughout the year, (3) optimal concomitant therapy with β_2 -agonists and/or methylxanthines, and (4) dependency on oral corticosteroid dosages of at least 10 mg of prednisone or 8 mg of methylprednisolone per day for at least 3 months before starting the study. If the minimal effective dose had not been previously determined, the investigator was required to lower the daily steroid dosage during a 3-month baseline period until asthma symptoms increased and thereby establish the minimal effective dose before randomization. To prevent confounding effects in determination of the "dependent dose," the use of high-dose inhaled corticosteroids (20 inhalations of beclomethasone or equivalent per day) was prohibited both during the baseline period and throughout the remainder of the study. However, standard doses of inhaled corticosteroids used before randomization were permitted.

Women of child-bearing potential were required to have a negative pregnancy test result and practice a clinically accepted method of contraception during the course of the study. Patients were excluded if: (1) they were younger than 18 years of age; (2) they had received previous treatment with gold compounds or had a history of gold-induced side effects; (3) allergen immunotherapy had recently been initiated; (4) they had received prior treatment with other steroid-sparing drugs (e.g., cromolyn, troleandomycin, methotrexate) within the previous 3 months; (5) they had smoked cigarettes within 6 months before the study; (6) they had been receiving fluctuating doses of oral corticosteroid drugs; (7) they had recent changes in inhaled corticosteroid dosages within 1 month preceding the study; and (8) there was clinical or laboratory evidence of serious concomitant systemic diseases.

Study design

This was a randomized, multicenter, double-blind, placebo-controlled, parallel-group clinical trial. Eligibility was determined at screening visits. Three months before randomization, there was a screening period during which the minimal effective corticosteroid dosage was established. Qualified patients entered a baseline 4-week lead-in period before randomization to treatment groups. During this interval, patients were evaluated for severity of asthma and for clinical stability with maintenance dosages. Fifty-five patients were excluded because of personal refusals, protocol violations, or failure to meet entry requirements. At the end of the baseline period, patients were randomized in approximately equal numbers to treatment with auranofin, 3 mg twice daily, or placebo for 28 weeks. The double-blind treatment period consisted of three consecutive phases: (1) a 12-week period, or phase I, during which oral corticosteroid dosages were not altered; (2) a 12-week period, or phase II, when weaning of oral corticosteroids was attempted according to a specific

reduction schedule; (3) a final 4-week observation period during which auranofin or placebo administration was continued along with either the reduced or unchanged oral corticosteroid dosage recorded at the end of phase II.

For the first 2 weeks of phase I, each patient received 1 capsule of auranofin (3 mg) or placebo per day, and subsequently the dose was increased to 2 capsules per day for the duration of active treatment. If the patient had an adverse experience that was possibly related to the coded medication, the investigator was allowed to decrease or temporarily discontinue the coded medication and reinstitute the study drug if the adverse experience resolved. If the same adverse experience recurred on reintroduction of the study drug, the patient was withdrawn from the study. The same dosages of patients' maintenance asthma medications, which were initiated before entry (i.e., β_2 -agonists, methylxanthines, and/or inhaled steroids), were maintained and not altered through the course of the study.

In the event of an acute flare-up, increases in oral corticosteroids were permitted. For patients receiving prednisone dosages of less than 20 mg per day at baseline, the dosage could be increased to 40 mg a day for no longer than 5 days. For patients receiving dosages of 20 mg or more per day, the dosage could be doubled for no longer than 5 days. A patient was withdrawn from the study if control of acute asthma flares required a dosage higher than 40 mg/day, durations of oral corticosteroids longer than 5 days, or more than two steroid bursts. During phase II, oral corticosteroid dosage was reduced every 2 weeks as long as patients were clinically stable or exhibited no increases in daytime or nocturnal asthma or in variability of peak expiratory flow rate. The following tapering schedule was used: (1) for patients who began receiving more than 30 mg of prednisone per day, the dose was reduced by 10 mg every 2 weeks; (2) for patients who began receiving a prednisone dosage of between 21 and 30 mg/day, a dose reduction of 5 mg every 2 weeks was permitted; (3) if the starting prednisone dose was 20 mg per day or less, a reduction of 2.5 mg every 2 weeks was allowed. The dosages of inhaled corticosteroids at baseline were not changed throughout the study in both treatment and placebo groups.

Global assessments of each patient's overall condition and response to treatment, ranging from very poor to very good (5-point scale) were made by both patients and physicians at week 12 of treatment and every 4 weeks thereafter. Symptom diaries, concomitant medication cards, and spirometry tests were assessed every 4 weeks. Daily self-administered morning and evening peak expiratory flow rates were collected. During the study, a complete blood count with differential, platelet counts, and urinalysis were performed monthly. Serum chemistries and total IgE were assessed during baseline and at weeks 12 and 28 of treatment.

Statistical methods

The primary efficacy end point for both treatment groups was therapeutic success, which was defined as a reduction of at least 50% from the baseline daily dose of oral corticosteroids before study entry. This parameter was analyzed in all patients, including those who did and those who did not complete the study. Secondary efficacy end points included: spirometric measurements, time to achieve maximal steroid reduction, time to improvement in pulmonary symptoms and lung function, asthma symptom scores, hospitalizations for treatment of asthma, β -agonist use, and physician and patient global assessments.

All statistical procedures for treatment comparisons were performed on an "intent-to-treat" basis and therefore included all patients randomized to auranofin and placebo groups. Statistical tests were two-sided, and results were considered statistically significant if *p* values were less than 0.05. The comparison of the primary efficacy variable was made by using Fisher's exact test. Crude event rates were analyzed by using Pearson chi-square techniques. Analyses of time to therapeutic success and of other clinical events (e.g., improvement in symptoms and FEV₁) were completed with life table techniques.

RESULTS

Of 334 patients screened, 140 were randomized to the auranofin group and 139 to the placebo group. Four patients in the auranofin group were excluded from the intent-to-treat efficacy analyses because of noncompliance in the initial 2 weeks of phase I. Therefore 136 patients were analyzed in the auranofin group. Eighty-two patients treated with auranofin and 75 patients treated with placebo completed the study. Forty-eight subjects withdrew because of adverse experiences: 47 because of protocol violations, 10 because of personal refusal to proceed, and 18 because of ineligibility. Table I lists the baseline clinical characteristics for patients randomized to treatment groups. Demographics, disease characteristics, and lung function were similar between groups. There were no significant differences in age, sex, duration of asthma, baseline maintenance dosages of oral prednisone, or use of inhaled steroids between the two intent-to-treat groups. In addition, there were no significant differences in baseline symptom scores, FEV₁, morning and evening peak expiratory flow rates, or β_2 -agonist requirements.

The primary efficacy end point was "therapeutic success," as defined by reduction of maintenance corticosteroid use by 50% or more. As shown in Table I, the therapeutic success of all treated patients who completed the study was significantly

TABLE I. Baseline patient characteristics before randomization to treatment

Characteristic	Placebo group (n = 139)	Auranofin group (n = 140)
Female (no., %)	68, 48.9%	65, 46.3%
Male (no., %)	71, 51.1%	75, 53.6%
Age in yr (mean $\pm$ SD)	50.47 $\pm$ 12.84	52.94 $\pm$ 13.45
Asthma duration in yr (mean $\pm$ SD)	17.88 $\pm$ 14.31	18.27 $\pm$ 15.51
Oral corticosteroid dose required before treatment		
<10 mg/day (no., %)	3, 22%	4, 2.9%
10–19 mg/day (no., %)	92, 66.2%	92, 67.7%
$\geq$ 20 mg/day (no., %)	44, 31.6%	40, 29.4%
Morning PEF (L/min)	297 $\pm$ 117	307 $\pm$ 113
Evening PEF (L/min)	348 $\pm$ 123	343 $\pm$ 115
FEV ₁ (% predicted)	64	63
Morning symptom score	1.4 $\pm$ 0.6	1.5 $\pm$ 0.6
Evening symptom score	1.5 $\pm$ 0.7	1.5 $\pm$ 0.6
Inhaled β -agonist		
Albuterol (mg)*	7.44 $\pm$ 7.40 (n = 85)	7.07 $\pm$ 8.23 (n = 95)
Metaproterenol (mg)*	69.67 $\pm$ 102.33 (n = 28)	34.5 $\pm$ 26.44 (n = 13)
Other β -agonists	Not tabulated† (n = 23)	Not tabulated† (n = 27)

*Mean accumulated dose during baseline.

†Not tabulated because of heterogeneity of drug use.

higher in the auranofin group compared with the placebo group (56 of 136 [41.2%] vs 37 of 139 [26.6%]; confidence interval, -25.7% to -3.5% ; $p = 0.01$). When all patients were analyzed, regardless of whether completion of the clinical trial was achieved, a significantly higher proportion of patients in the auranofin group achieved 50% reduction of baseline corticosteroid dosages compared with patients in the placebo group (76 of 136 [55.9%] vs 45 of 139 [32.4%]; confidence interval, -34.9% to -12.1% ; $p < 0.001$). These effects occurred without concurrent increase in asthmatic symptoms or exacerbations or deterioration in pulmonary function.

Therapeutic success was associated with the baseline maintenance oral corticosteroid dosage. As shown in Table II, the effect of auranofin on steroid reduction was most remarkable in the group of patients receiving baseline doses ranging from 10 to 19 mg of oral prednisone per day ($p < 0.001$). Analysis of all treated patients revealed a trend for therapeutic success in the auranofin group receiving 20 mg of prednisone or more per day at baseline (19 [47.5%] vs 12 [27.3%]; $p < 0.06$), but this did not reach statistical significance. In the group of patients who did not complete the study, therapeutic success was also higher in those treated with auranofin (10 to 19 mg group: 10 of 47 [21%]; ≥ 20 mg group: 9 of 30 [30%]) than in those treated with placebo (10 to 19 mg group: 5 of 66 [7%]; ≥ 20 mg group: 3 of 35 [8%]).

Kaplan-Meier analysis was used to analyze the survival distribution of the two groups in achieving a 50% reduction in the daily maintenance dose of prednisone. According to the log-rank test, there was a significant overall difference between the two treatment groups because of the overall higher response rate in the auranofin group ($p = 0.03$). There was no difference between auranofin and placebo responders in the time to achieve therapeutic success because the mean time to achieve 50% reduction in oral corticosteroids (16.5 weeks) was similar for both treatment groups. No other significant factors or treatment-by-factor interactions were found for sex, race, age, type of asthma, baseline emergency department visits, baseline exacerbations, baseline hospitalizations, or duration of asthma.

There were no significant differences between treatment and placebo groups in pulmonary symptoms, peak expiratory flow rates, FEV₁, lung volumes, and concomitant asthma therapy. In particular, there was no significant difference in the use of inhaled corticosteroids between groups ($p = 0.98$). The auranofin group had a significantly greater change or improvement in the mean patient global assessment score than did the placebo group ($p = 0.02$). There was no significant difference between treatment groups with respect to the changes in physician global assessment ($p = 0.47$).

During the 4-week observation period (weeks 24 to 28), doses of oral corticosteroids and study

TABLE II. Therapeutic success in all patients randomized to treatment classified by baseline oral corticosteroid dose before treatment

Treatment group	Dose at randomization (mg)	Total randomized (n)	Therapeutic success			
			Completed study patients		Completed + noncompleted study patients*	
			No.	%	No.	%
Placebo	<10	3†	2	66.7	2	66.7
	10–19	92	26	28.3	31	33.7
	≥20	44	9	20.5	12	27.3
Auranofin	<10	4†	1	25.0	2	50.0
	10–19	92	45	48.9‡	55	59.8§
	≥20	40	10	25.0	19	47.5

Therapeutic success was defined as ability to reduce maintenance oral corticosteroids by at least 50% from the maintenance dosage at randomization.

*This is the intent-to-treat analysis, which includes all patients randomized to treatment, both those who did and those who did not complete the entire 28-week protocol.

†Not analyzed because of incorrect entry dosage.

‡Auranofin versus placebo $p < 0.01$.

§Auranofin versus placebo $p < 0.001$.

||Auranofin versus placebo $p < 0.06$.

drugs were not altered. There were no significant differences between auranofin and placebo groups in asthma symptom scores, lung function, or use of concomitant medications (e.g., β -agonists, inhaled steroids). There were no withdrawals between weeks 24 and 28 as a result of asthma exacerbations.

The safety evaluation was based on adverse events recorded for 279 patients randomized to treatment groups. Adverse experiences resulted in permanent discontinuation of coded medication in 25 of 140 (17.1%) patients in the auranofin group and in 23 of 139 (16.5%) patients in the placebo group. It was noteworthy that six patients treated with auranofin and 11 patients treated with placebo were withdrawn from the study because of asthma exacerbations requiring use of steroids in excess of those permitted by the protocol. Hospitalization was required for 18 of 140 (12.8%) patients treated with auranofin and 20 of 139 (14.4%) patients treated with placebo. Hospitalization was due to exacerbation of asthma symptoms in nine of 17 (52.9%) patients treated with auranofin and in seven of 19 (36%) patients treated with placebo. One male patient treated with auranofin died as a result of respiratory failure related to a severe exacerbation of asthma. This patient had experienced a prior episode of respiratory failure. Before the fatal event, he had been receiving prednisone (10 mg/day) and received auranofin, 3 mg twice daily, for 13 weeks. The patient had

experienced an increase in asthma symptoms at week 13 of treatment but did not report changes in his symptoms to the clinical investigator. An autopsy was not performed.

Table III summarizes adverse experiences that were not related to asthma encountered in more than 5% of patients in both auranofin and placebo groups. There was no significant difference between the two treatment groups with respect to nonasthmatic adverse events that resulted in discontinuation of coded medication ($p = 0.47$). As expected, the auranofin group had significantly more gastrointestinal and dermatologic adverse experiences than the placebo group; (gastrointestinal [60.0% vs 31.8%, $p < 0.001$], skin [30.0% vs 16.6%, $p = 0.015$], and for the body as a whole [37.9% vs 28.8%, $p = 0.008$]). Two serious gastrointestinal events (one non-drug-related case of diverticulosis with perforation and one drug-related case of gastroenteritis and gastrointestinal hemorrhage) occurred in the auranofin group, and one non-drug-related gastrointestinal event (perforation of the large intestine) occurred in the placebo group.

There were no significant changes in hematologic or hepatic clinical laboratory parameters. One auranofin-treated patient who had proteinuria required withdrawal after week 21 of treatment. The mean serum total IgE level was significantly decreased from baseline in the auranofin group (-44.63 IU/ml, $p = 0.003$) compared with the placebo group (13.1 IU, $p = 0.223$).

TABLE III. Adverse experiences reported in 5% or more of patients according to medication regimen

Adverse experience	Auranofin (n = 140)	Placebo (n = 139)
Body as a whole (general)		
Chest pain	9 (6.4%)	7 (5.0%)
Fatigue	13 (9.3%)	7 (5.0%)
Fever	7 (5.0%)	4 (2.2%)
Injury	7 (5.0%)	4 (2.2%)
Pain	7 (5.0%)	4 (2.9%)
Central and peripheral nervous system		
Headache	31 (22.1%)	33 (23.7%)
Gastrointestinal system		
Abdominal pain	19 (13.6%)	6 (4.3%)
Diarrhea	61 (43.5%)	26 (18.7%)
Dyspepsia	15 (10.7%)	13 (9.4%)
Flatulence	7 (5.0%)	4 (2.9%)
Nausea	14 (10.0%)	10 (7.2%)
Musculoskeletal system		
Arthralgia	13 (9.3%)	2 (1.4%)
Myalgia	8 (5.7%)	5 (3.6%)
Host resistance		
Viral infection	12 (8.6%)	11 (7.9%)
Sinusitis	26 (18.6%)	28 (20.1%)
Upper respiratory tract infection	37 (26.4%)	38 (27.3%)
Respiratory disorder	2 (1.4%)	10 (7.2%)
Skin and appendages		
Pruritus	13 (9.3%)	6 (4.3%)
Rash	12 (8.6%)	8 (5.8%)
Urinary system		
Albuminuria	12 (8.6%)	10 (7.2%)
Hematuria	14 (10.0%)	14 (10.1%)
Urinary tract infection	8 (5.7%)	9 (5.8%)
White cell and reticuloendothelial system		
Lymphopenia	9 (6.4%)	5 (3.6%)

DISCUSSION

Evaluation of the steroid-sparing effects of a novel drug in the treatment of steroid-dependent asthma has been approached from two perspectives: (1) drug evaluation while patients continue to receive a maintenance or minimally effective dose of oral corticosteroids³ or (2) deliberate reduction of maintenance corticosteroid dosages after patients have been stabilized while receiving the steroid-sparing drug.² Improvement in symptoms and lung function have been the primary efficacy end points for the first approach, whereas the primary outcome measure for the second ap-

proach has been successful corticosteroid reduction, often without concomitant change in asthmatic symptoms or lung function. The latter approach was chosen in this investigation.

Auranofin was significantly superior to placebo in reducing the total oral corticosteroid dosage requirements. The effect of auranofin was significant in all treated patients but particularly in a group of patients who required 10 to 19 mg of oral corticosteroids per day during the prestudy baseline period. Although there was a strong trend toward therapeutic success in the patient group receiving 20 mg of prednisone or more per day, statistical significance was not attained. Apart from the smaller number of patients in this category, a possible explanation for the poorer response may be that patients requiring daily doses of at least 20 mg of prednisone may have reached an advanced stage of disease at which antiinflammatory agents are less likely to exert a steroid-sparing effect. Thus it may be necessary to consider use of auranofin or other antiinflammatory agents earlier in the treatment of patients with steroid-dependent asthma.

Because of the study design, it was not surprising that secondary efficacy variables, such as respiratory symptoms and FEV₁, did not differ between treatment groups. Nevertheless, patient global assessment was significantly better for the auranofin group than for the placebo group ($p = 0.02$). Interpretation of clinical results in any steroid reduction protocol is highly dependent on the reliability of achieving the lowest, clinically effective corticosteroid dose for each patient before randomization to active treatment.¹⁶ In this trial special inclusion provisions were made to document that each patient had achieved the lowest, optimal corticosteroid dose before randomization to treatment. Despite this rigid entry criterion, some patients in the placebo group were able to further reduce steroid dosage during the treatment period. This same effect had been noted previously in a steroid-sparing asthma trial of methotrexate, which was explained by closer patient-physician interactions that could improve patient compliance.¹⁶ This finding reinforces the necessity of using the parallel placebo-controlled design for evaluation of steroid reduction in patients with severe asthma.

The steroid-sparing effects of auranofin in this study are similar to those observed in an open pilot study conducted in the United States.¹³ The clinical observations in this study also confirmed results obtained in a smaller placebo-controlled study (26 weeks) of auranofin by Nierop et al.¹⁴ in 32 pa-

tients with asthma requiring oral corticosteroids. In this trial a 50% reduction in oral corticosteroid requirements was achieved in 87% of auranofin-treated patients who required at least 2.5 mg of prednisone per day. The greater success rate of the earlier study is likely attributable to a population of patients with less severe asthma whose corticosteroid maintenance dosage requirements at entry were lower than those in this trial.

Elevations in serum total IgE have been demonstrated in asthmatic populations and appear to be independent of atopic status.¹⁷ Reduction of total IgE in patients treated with auranofin in this trial confirmed other previous reports.^{12, 13} The mechanism of this interesting observation is unknown, and it remains to be determined whether reduction in serum total IgE levels in patients treated with auranofin is predictive of therapeutic outcome.

The analysis of adverse experiences indicated that the auranofin group had a significantly higher incidence of gastrointestinal, dermatologic, and other nonspecific (fatigue, fever, pain) adverse events. Most of the gastrointestinal complaints consisted of diarrhea or loose stools and improved after temporary reduction of the daily auranofin dosage. It is apparent that the occurrence of major side effects, such as gastrointestinal disturbances, rash, and pruritus, appears to be similar in patients treated for asthma and rheumatoid arthritis. Stomatitis was not encountered in this asthma study. It should be emphasized that the chief gastrointestinal adverse event was diarrhea, which could be controlled by reduction of the auranofin dosage or in some cases by stopping the drug administration temporarily and resuming it at a later date. Subsequently, many patients were able to resume the full 6 mg daily dose. The type, incidence, and severity of other gold-associated adverse events observed in this study did not differ from those observed in other asthma or rheumatoid arthritis clinical trials with auranofin.^{5, 6, 13, 14, 18}

In summary, this placebo-controlled study of auranofin in the management of chronic steroid-dependent asthma revealed that this oral gold drug clearly has a steroid-sparing effect without concomitant worsening of symptoms or objective lung function test results. The risk-benefit results encountered in the study demonstrated that this drug has an acceptable safety and efficacy profile when weighed against the considerable side effects of long-term administration of oral corticosteroids. Before patients who are dependent on oral corti-

costeroids are considered for auranofin treatment, every effort should be made to optimize and maximize inhaled corticosteroid treatment, which might allow reduction or discontinuation of oral steroids. The results of this study suggest that auranofin should be useful for patients with asthma requiring moderate doses of oral prednisone or methylprednisolone.

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