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Irritability in Autistic Children Treated with Fenfluramine

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reported for Feldene exceeds that reported to the System for benzoxa-
profen (Oralac), a structurally unrelated nonsteroidal antiinflam-
matory agent that has been withdrawn from the market. The origi-
nal package insert for Feldene does not list photosensitivity as an
adverse reaction associated with its use. Yet 29 of 36 reactions asso-
ciated with this drug were clearly consistent with photosensitivity
reactions, and 2 of the remaining 7 reports of reactions were highly
suggestive of exacerbation by exposure to sunlight. The 29 patients
who had photosensitive eruptions (16 men and 13 women) ranged
in age from 20 to 74 years; one patient (a man) was black. In 19 of
the 29 patients the eruption occurred within four days and after
their first sun exposure after the initiation of Feldene therapy. A
majority of the cases included vesicles or bullae in sun-exposed
areas. Pruritus was frequently associated with the eruption.

The prompt onset of the eruption in relation to initial treatment
and sun exposure suggests a phototoxic rather than a photodermal
reaction. Three patients who had used thiazide diuretics for ex-
tended periods of time experienced photosensitivity reactions after
Feldene was added to their therapeutic regimen, suggesting possi-
ble additive or synergistic phototoxic effects of Feldene and
thiazides.

Robert S. Stern, M.D.
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The above letter was referred to Pfizer Laboratories, manufac-
turers of Feldene, who offer the following reply:

To the Editor: Although Dr. Stern correctly notes that the original
Feldene (piroxicam) package insert did not list photosensitivity re-
actions, they were added in August 1982, three months before we
received a communication from him. We made this change volun-
tarily, because we had received reports of such reactions (including
cases from Dr. Stern) after Feldene was introduced, even though we
had not seen them in more than 1000 patients studied in our con-
trolled clinical trials. We believe that our current labeling, which
states that these reactions occur in fewer than 1 per cent of patients,
is supported by this experience.

Some government agencies, such as the Committee on Safety of
Medicines in the United Kingdom and the Swedish Regulatory
Authority, routinely report information on adverse reactions. Data
from these agencies suggest that the incidence of photosensitivity
reactions with Feldene is probably on the same order of magnitude
as the incidence with other marketed nonsteroidal antiinflammatory
drugs, including ibuprofen, indomethacin, and naproxen.

Pfizer has recently reviewed side effects in over 70,000 patients
around the world who were treated with Feldene, as well as in com-
parative studies with indomethacin and naproxen. Dermatologic
reactions of any kind occurred in about 1 to 3 per cent of patients
and had a similar incidence with each of the drugs.

Finally, it should be noted that benoxaprofen was withdrawn
from the market because of hepatic and renal toxicity, not because
of photosensitivity, as implied in Dr. Stern's letter.

New York, NY 10017

Roger Sachs, M.D.
Pfizer Laboratories

Irreliability in Autistic Children Treated
With Fenfluramine

To the Editor: A report by Geller et al. presented preliminary
results suggesting the possible usefulness of fenfluramine (a substi-
tuted phenethylamine widely used as an appetite suppressant) in
the treatment of infantile autism (July 15, 1982, issue). The raison-
dable for the use of this agent rests on its ability to lower peripheral-
level blood levels of serotonin and on the observation that a substantial
minority of autistic patients have elevated peripheral-blood sero-
tonin levels.1 The report emphasized the preliminary nature of the
results in a small sample of three young autistic boys with elevated
serotonin levels. We have seen two cases in which autistic children
were treated with this agent and appeared to have adverse reactions
to it. In neither case was peripheral serotonin measured before

A seven-year-old boy had been diagnosed as autistic at the age of
five. The child had a variety of the features typical of autistic chil-
dren and was enrolled in a special-education program. His pediat-
rician had given him fenfluramine, 10 mg four times a day. During
one month of treatment with this agent the child became progres-
sively irritable and fearful. His activity level increased and his
appetite decreased. Sleep was also disrupted. He deteriorated be-

behaviorally, and his family discontinued the medication. At our
examination, performed two months after treatment had been
stopped, his serotonin levels were not elevated (152 ng per milli-
liter).

An 11-year-old autistic boy had been started on fenfluramine (10
mg four times a day) by his father, who had read the preliminary
report by Geller et al. Serotonin levels were not determined before
treatment. Over several days of treatment the child became more
irritable and agitated. Fenfluramine was discontinued. The boy's
activity level was markedly increased during the initial treatment,
and his father sought an examination. At our examination, one month
after treatment had been discontinued, the child had a serotonin
level of 212 ng per milliliter.

Adverse reactions to fenfluramine have been noted previously.2

In one double-blind investigation the efficacy of this agent as an
appetite suppressant was evaluated; both patients and physicians
were able to identify the active agent correctly in over 70 per cent of
cases — largely on the basis of side effect.3

There is no rationale for the use of fenfluramine in autistic chil-
dren who do not have elevated levels of serotonin. Furthermore,
its efficacy in this population remains to be clearly established. Phy-
sicians should be aware of possible adverse effects of this agent in
autistic children and its investigational nature.

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Cimetidine and Polymyositis

To the Editor: Watson et al. recently reported a case of polymyositis
induced by cimetidine, a drug with a possible role as an immuno-
modulator (Jan 20 issue). Since November 1982, we have had the
opportunity to follow the patient described in their report and wish
to provide follow-up data that argue against the role of cimetidine
in inducing polymyositis in this patient.

Although cimetidine had been discontinued in January 1982, the
patient had active myositis when first seen by us. In January 1983,
while taking prednisone (30 mg per day) and mercaptopurine (50
mg three times a day), he had a severe exacerbation of myositis
with profound weakness and elevation of creatine kinase to 289,000
IU per liter. He denied using cimetidine or alcohol. Since then his
myositis has remained active despite treatment with high doses of
prednisone and mercaptopurine.

It is apparent that 15 months after discontinuation of cimetidine,
this patient continues to have progressive polymyositis. This con-
trasts sharply with previously reported cases of drug-induced poly-
myositis, in which remission of disease was observed soon after
discontinuation of the drug. For example, in all previously reported
cases of penicillamine-associated polymyositis, remission or marked
improvement in both clinical and laboratory features of the disease
occurred within six months of stopping the drug.4 In no case was

1. Geller E, Ricks ER, Freeman BJ, Yuwiler A. Preliminary observations on
the effect of fenfluramine on blood serotonin and symptoms in three autistic

2. Hanley HG, Stahl SM, Freedman DX. Hyperserotonemia and amine metabo-


4. Brownell KD, Stunkard AJ. The double-blind in danger: untoward conse-