Page 1, par. 3 line 4:

Substitute: "but such agents have an addiction potential with long term use except in those individuals with a history of addiction or barbituation to narcotics in the past."

Instead of: "but such agents are frequently over constipating and they have a recognized addicting potential."

A double blind study concluded 2.5 mg. Lomotil was effective as 4 cc. of camphorated tincture of opium (Barowsky and Schwartz). Codeine was preferred by a few patients to Lomotil (Bachrach and Voigtlin). Codeine, tincture of opium and other narcotics are not more constipating than Lomotil, a congener of meperidine (Demerol).

The addiction potential of a narcotic is type, time and dose related. The longer the use of a narcotic the greater the addiction or abuse potential. *The only advantage of Lomotil, in therapeutic doses only, over the use of other narcotics for the treatment of a symptom, chronic diarrhea, it is minimal addicting potention on long term use.*

Page 2 Clinical Application: line 1 delete "excessive" after "undergone."

Line 2: Substitute: "It, as an adjuvant to specific therapy and a general treatment program" for: "It is the sole treatment or as part of a general treatment program."

Line 12: Add after "regional enteritis" mild. It has been shown that moderate and severe inflammatory disease of the intestinal tract, e.g. regional enteritis, ulcerative colitis, acute ileitis of varying etiologies, etc., react poorly, if at all, to the administration of Lomotil and other narcotics.

A compensated incomplete intestinal obstruction secondary to the intrinsic granulamatous disease process of regional enteritis may be converted to a complete obstruction by the use of this drug; and, an ileus created in ulcerative colitis. (Sleisinger and Almy)

Line 14: Add "mild" after "ulcerative colitis". Poor results were reported in the use of Lomotil in moderate and severe ulcerative colitis. Precaution must be exercised in the use of the drug to obviate ileus with possible complicating toxic megacolon, perforation, etc.

Page 3, par. 2 line 3 beginning "Machella" change "6" to "8".

Line 4: Change "9" to "8".

Line 17: Add, after "seen no undesirable sequelae", the statement: "There were no efficacious results even with high dosage (40 mg. daily) in sprue, regional enteritis and fair to poor results in 5 cases of ulcerative colitis".

Line 18: After "have ever used" add in parenthesis (1 case). The testimonial of one case questions the accompanying quote of "it is the best I have ever used" in the brochure.

Page 5 par. 1 line 8: After "treatment" add 8 patients benefited from treatment. See authors summary and conclusions.

Par. 2 line 6: Add "which is generally a self limiting disease" instead of "effect in acute diarrhea."

Dosage—Children: *Delete entire section.*

No studies have been performed using diphenoxylate hydrochloride with 0.05 mg. atropine sulfate in children. The uncontrolled studies on children were accomplished using R1135 (diphenoxylate hydrochloride). Adverse reactions, including deaths, have been reported in children using therapeutic doses. Furthermore, fraction of tables and teaspoons (varying from 4–5 cc.) are really not proper dosage forms for children who are very sensitive to the action of atropine.

Par. 6—Side effects: Add: headache, lightheadedness, toxicosis, angioneurotic edema, giant urticaris, lethargy, anorexia, atropine effects, respiratory difficulty and coma.

NOTE.—The statement that "Side Effects are relatively rare" is not accurate e.g.:
Schwartz, 24 side effects in 53 pts. 24/53.
Bachrach, 2 side effects in 6 pts. 2/6.
Voigtlin, 5 side effects in 11 pts. 5/11.
Klotz, 4 side effects in 24 pts. 4/24.
Texter, 3 side effects in 15 pts. 3/15.
McGlone, 5 side effects in 24 pts. 5/24.

(Severe enough to withdraw drug)

European study, 24/364.

This does not constitute, in any language, statistically or otherwise infrequent reactions, nor can one justify the appellation of "relatively rare" to the number and type of reactions. Nausea, as one (1) symptom, was corrected in many instances by withdrawing the drug or reducing the dose. Can this deserve the statement that most cases of nausea were due to the underlying condition or it is apparent the drug contributed its share to the production of nausea in both adults and children?