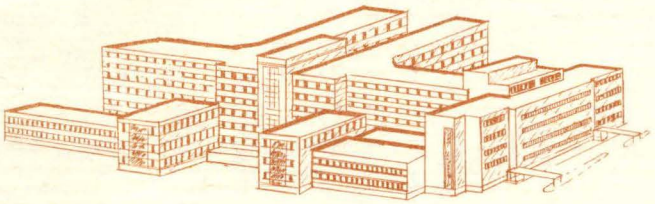

THE MOSES H. CONE MEMORIAL HOSPITAL

GREENSBORO, NORTH CAROLINA

PHARMACY COMMITTEE NOTES

VOLUME IX - Number 4 August 1977

DRUG-INDUCED ENTEROCOLITIS

The occurrence of pseudomembranous colitis, following administration of various drugs, predominantly antibiotics, is well recognized. Usually, the gastrointestinal symptoms become manifest four to six days after initiation of antibiotic therapy. These symptoms include nausea, vomiting, anorexia, abdominal discomfort, and most prominently, diarrhea. The latter is usually moderate, but occasionally the surge of fluids and electrolytes into the alimentary tract is overwhelming and life threatening.

In the more severe condition, the intestinal tract is usually dilated and filled with liquid feces. The mucosal surface is generally lined with a friable, adherent, white, tan, or greenish pseudomembrane that occurs in isolated plaques or as an extensive confluent process. The membrane can be easily separated from the underlying mucosa, which is usually ulcerated, congested, and edematous.

Microscopically, the membrane consists of necrotic cellular debris, fibrin, mucus, and a variable number of inflammatory cells. Occasionally, bacteria and fungi are identified. As the disease progresses, the mucosa can undergo a coagulative necrosis which will eventually lead to massive ulceration and possible perforation.

The most common factor producing these manifestations is the use of oral and parenteral broad-spectrum antibiotics. However, the incidence with parenteral therapy is much lower. Slagle et al.,[1] as a result of a poll of the American Society of Colon and Rectal Surgeons, developed a list of antibiotics which have been implicated as having been responsible for this disease. The list goes from most prevalent to least:

(1) Clindamycin
(2) Lincomycin
(3) Tetracycline
(4) Ampicillin
(5) Erythromycin
(6) Penicillin
(7) Neomycin
(8) Cephalexin
(9) Cephalothin
(10) Bactrim®, Septra®

In each instance, the diagnosis was established by careful history, physical exam, procto-sigmoidoscopic examination, smear, gram stain, and cultures. In each of these cases, the severity of the disease was not dose related; however, those patients who were continued on the antibiotics in spite of G.I. irritations had a more prolonged course of the disease.

There has been much speculation as to the etiology of the disease, but to date the specific course is still unknown. Shapiro et al.[2] have theorized several concepts as to why antibiotics cause this syndrome. They found 50 percent of the authenticated cases can be attributed to demonstrable staphylococcal infection. The indiscriminant use of broad spectrum antibiotics raises the incidence of staphylococcal enterocolitis. These same antibiotics were also shown to induce changes of the normal bacterial flora leading to an overgrowth of resistant pathogenic organisms. A third theory of Shapiro's is that ischemia due to peripheral circulatory collapse was the cause of colitis. However, many clinicians feel that circulatory failure is a consequence of enterocolitis rather than a cause. Lastly, they felt that the antibiotic, or one of its metabolites, might have a direct mucosal toxic effect; and that via enterohepatic circulation, the antibiotic causes a continuous irritation.

The mainstay of therapy is cessation of the precipitating factor and correction of physiologic abnormalities. The most severe cases require vigorous fluid and electrolyte replacement, albumin, whole blood, nasogastic suctioning, and often corticosteroid therapy. Tedesco et al.[3] treated all their patients with Lomotil®, discontinuation of antibiotics, and general supportive care. Their clinical courses included disappearance of cramps--usually within 48 hours--and a gradual improvement of diarrhea. In most serious conditions, ACTH and hydrocortisone retention enemas were instituted into the regimen and have elicited striking results. Burbage and Milligan[4] reported good results when using cholestyramine powder. They found that with a regimen of cholestyramine, 4 Gm. three times daily, that the frequency of bowel movements decreased over the ensuing two days; and by the third day of treatment, the patients were having formed stools. The mechanism by which cholestyramine

worked on these patients is not clear. It may be that there is bile acid malabsorption in antibiotic-associated pseudomembranous colitis. It is this increased concentration of secondary bile acids which contributes to diarrhea. As an anion exchange resin, cholestyramine binds bile acids, thus reducing the likelihood of a bile acid-induced diarrhea.

Drug-induced colitis must be an important consideration in any patient recently receiving antibiotics who develops fever, abdominal pain and diarrhea. The disease can be self-limiting when the diagnosis is made early and the offending drug is immediately stopped. The diagnosis can be readily substantiated by careful proctoscopic examination. To prevent a disease that is seriously debilitating, an immediate diagnosis is necessary and removal of the offending agent is foremost.

REFERENCES

1. Slagle, G. W. et al.: Drug-Induced Pseudomembranous Enterocolitis, Dis. Col. and Rect., 19:253, 1976.
2. Shapiro, R. L.: Acute Enterocolitis, Radiology, 108:263, 1973.
3. Tedesco, F. J. et al.: Clindamycin-Associated Colitis, Am. Int. Med., 84:429, 1974.
4. Burbage, E. J. et al.: Pseudomembranous Colitis, JAMA, 1157:231, 1975.

ANABOLIC STEROIDS

A number of anabolic steroids were removed from the hospital formulary after a review of this class of drugs by the Pharmacy Committee. The preparations removed are infrequently used and are similar to drugs remaining in the formulary.

Deleted drugs:

Methyltestosterone - Oreton Methyl®
Ethylestrenol - Maxibolin®
Methandrostenolone - Dianabol®
Oxandrolone - Anavar®
Oxymetholone - Anadrol®, Adroyd®
Stanozolol - Winstrol®

Anabolic steroids remaining in formulary and routinely stocked by the pharmacy:

Fluoxymesterone - Halotestin®
Testosterone - Delatestryl®
Nandrolone - Durabolin®, Deca-Durabolin®

INFLUENZA VIRUS VACCINE FOR 1977-1978

The Bureau of Biologics of the FDA has issued its recommendation for the influenza virus vaccine 1977-1978. A bivalent influenza vaccine composed of 400 chick cell agglutinating (CCA) units per adult dose will be used. Each dose will contain 200 CCA units of type A/Victoria/3/75 (H3N2) and 200 units of type B/Hong Kong/5/72 influenza virus.

This year's vaccine is available as both the "split-virus" and "whole-virus." The split-virus vaccine appears to have fewer side effects than the whole-virus vaccine, especially in children. It is not as effective as the whole-virus vaccine in stimulating antibody production when given as a single dose to persons not previously exposed to related antigens by infection or vaccination.

Most adults and older children have had some exposure to antigens related to the types A/Victoria and B/Hong Kong. They should have a good antibody response to a single dose of the 1977-1978 bivalent influenza vaccine. Children under six years of age may not have been previously exposed to these antigens and will need two doses of vaccine given four weeks apart.

A vaccination is strongly recommended for persons of any age who have chronic conditions such as heart disease of any etiology, chronic bronchopulmonary diseases, chronic renal disease, and diabetes mellitus or other chronic metabolic disorders. Also, any person over 65 years of age should receive that vaccine.

The vaccine available for use at Moses Cone Hospital is Fluogen® by Parke-Davis, the bivalent split-virus vaccine containing 200 CCA units of type A/Victoria and 200 CCA units of type B/Hong Kong per 0.5 ml. dose. The dosages to be used for the 1977-1978 influenza season, as recommended by the Bureau of Biologics, are: children 6-35 months, two injections of 0.15 ml. each, separated by four weeks or longer; children 3-5 years old, two injections of 0.25 ml. each, separated by four weeks or longer; 6 years and older, one injection of 0.5 ml.

Visconti, J. A.: Influenza Virus Vaccine For 1977-1978, The White Sheet, July 1977.