

A NURSING ASSESSMENT TOOL FOR FOLLOW-UP
CARE OF ANTIBIOTIC-INDUCED
PSEUDOMEMBRANOUS COLITIS

A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF
THE REQUIREMENTS FOR THE DEGREE
OF MASTER OF SCIENCE IN THE
GRADUATE SCHOOL OF THE TEXAS
WOMAN'S UNIVERSITY

COLLEGE OF NURSING

BY

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AUGUST 1977

The Graduate School
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June 24 19 77

We hereby recommend that the thesis prepared under
our supervision by Daniel J. Werlinger
entitled "A Nursing Assessment Tool for Follow-up Care
of Antibiotic-Induced Pseudomembranous Colitis"

be accepted as fulfilling this part of the requirements for the Degree of
Master of Science.

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DEDICATION

To the ones in my life that made this all come true:

My mother, Jo Werlinger, a woman who always had time to listen, inspire me and love me. My father, Al Werlinger, a man that I dearly love and respect, who gave me the will and stamina to keep working at anything I try.

My wife, Paula, a woman that has given me great joy and love, who has endured great hardships, frustration and loneliness while I continued my education. My grandmother, Florence, a woman who taught many things about life, one of these being love. My only wish is that she were here to enjoy this accomplishment.

My other loved ones, Robert and Dean Bowers, two people I love very dearly and who treat me as their child. Who, like the rest, have endured with me these trying times. My advisor and friend, Robert Raszkowski, whose unselfishness and understanding helped me to get to this point in my life.

And finally to God, for giving me the strength to continue when the odds seemed so insurmountable.

To all of these people, I thank you and I hope that through this I may assist others that need help also.

ACKNOWLEDGEMENT

It is with the deepest sense of gratitude that I acknowledge those who assisted me in my study:

Members of my thesis committee:

Mona Counts, R.N., Ph.D.

Robert R. Raszkowski, Ph.D., M. D.

Delores Sawyer, R.N., M. S.

I would like to thank my family for all the encouragement and support provided by them during the preparation of this paper .

Dan Werlinger

TABLE OF CONTENTS

	Page
DEDICATION	iii
ACKNOWLEDGEMENT	iv
TABLE OF CONTENTS	v
LIST OF TABLES	viii
 CHAPTER	
I INTRODUCTION	1
Statement of the Problem	3
Purposes of the Study	3
Background and Significance	4
Definition of Terms	5
Limitations	8
Delimitations	8
Assumptions	9
Summary	9
Overview of the Following Chapters	10
II REVIEW OF LITERATURE	11
Introduction	11
Antibiotics as Causative Agents in	
Pseudomembranous Colitis	14
Ampicillin	15
Tetracycline	16
Lincomycin and Clindamycin	17
Clinical Features	20
Laboratory data	21

	Page
Therapy	23
Clinical Nurse Specialist	25
Summary	28
III PROCEDURE FOR COLLECTION AND TREATMENT OF DATA	30
Setting	30
Population	31
Tool	31
Collection and Treatment of Data	31
Summary	32
VI ANALYSIS OF DATA	34
Introduction	34
Incidence	34
Causative Antibiotic Agents	39
Chief Complaints and Clinical Manifestations	45
Previous Bowel History	52
Reasons for Antibiotic Therapy	53
Physical Examination	59
Initial Diagnosis	62
Laboratory Data	65
Therapy	73
Follow-up Care and Outcome	79
Summary	80
V SUMMARY, CONCLUSIONS, IMPLICATIONS, AND RECOMMENDATIONS	83
Summary	83
Conclusions	84
Implications	87
Recommendations	89
APPENDICES	
A PERMISSION FOR THE STUDY	91

	Page
B CRITERION	93
C ASSESSMENT TOOL	95
BIBLIOGRAPHY	98

LIST OF TABLES

		Page
1	AGE, SEX, AND RACIAL DISTRIBUTION OF CASES WITH ANTIBIOTIC-INDUCED PSEUDOMEMBRANOUS COLITIS FROM LITERATURE REVIEWED	36
2	AGE AND SEX OF CASES WITH ANTIBIOTIC-INDUCED PSEUDOMEMBRANOUS COLITIS IN STUDY HOSPITAL JANUARY 1970 - JUNE 1977	38
3	ANTIBIOTIC CAUSATIVE AGENTS OF CASES WITH ANTIBIOTIC-INDUCED PSEUDOMEMBRANOUS COLITIS FROM LITERATURE REVIEWED	40
4	ANTIBIOTIC CAUSATIVE AGENTS OF CASES WITH ANTIBIOTIC-INDUCED PSEUDOMEMBRANOUS COLITIS IN STUDY HOSPITAL JANUARY 1970 - JUNE 1977	43
5	CLINICAL FEATURES OF CASES WITH ANTIBIOTIC-INDUCED PSEUDOMEMBRANOUS COLITIS IN REVIEWED LITERATURE	47
6	CLINICAL FEATURES OF CASES WITH ANTIBIOTIC-INDUCED PSEUDOMEMBRANOUS COLITIS IN STUDY HOSPITAL JANUARY 1970 - JUNE 1977	49
7	REASONS FOR RECEIVING ANTIBIOTICS OF CASES WITH ANTIBIOTIC-INDUCED PSEUDOMEMBRANOUS COLITIS FROM REVIEWED LITERATURE	54
8	REASONS FOR RECEIVING ANTIBIOTICS OF CASES WITH ANTIBIOTIC-INDUCED PSEUDOMEMBRANOUS COLITIS IN STUDY HOSPITAL JANUARY 1970 - JUNE 1977	57

	Page
9 INITIAL PHYSICAL EXAMINATION FINDINGS OF CASES WITH ANTIBIOTIC-INDUCED PSEUDOMEMBRANOUS COLITIS IN REVIEWED LITERATURE	60
10 INITIAL PHYSICAL EXAMINATION FINDINGS OF CASES WITH ANTIBIOTIC-INDUCED PSEUDOMEMBRANOUS COLITIS IN STUDY HOSPITAL JANUARY 1970 - JUNE 1977	63
11 HEMATOLOGIC FINDINGS OF CASES WITH ANTIBIOTIC- INDUCED PSEUDOMEMBRANOUS COLITIS IN STUDY HOSPITAL JANUARY 1970 - JUNE 1977	67
12 RADIOLOGIC FINDINGS OF CASES WITH ANTIBIOTIC- INDUCED PSEUDOMEMBRANOUS COLITIS IN REVIEWED LITERATURE	69
13 RADIOLOGIC FINDINGS OF CASES WITH ANTIBIOTIC- INDUCED PSEUDOMEMBRANOUS COLITIS IN STUDY HOSPITAL JANUARY 1970 - JUNE 1977	71
14 TREATMENT MODALITIES OF CASES WITH ANTIBIOTIC-INDUCED PSEUDOMEMBRANOUS COLITIS IN REVIEWED LITERATURE	74
15 TREATMENT MODALITIES OF CASES WITH ANTIBIOTIC-INDUCED PSEUDOMEMBRANOUS COLITIS IN STUDY HOSPITAL JANUARY 1970 - JUNE 1977	77

CHAPTER I

INTRODUCTION

The past century has seen great advances in the field of medicine. One of the most far reaching of these advances has been the development of antibacterial chemotherapy. Prior to the late 1930's, many patients died from a multitude of infectious diseases. The discovery of the sulfonamides and penicillin opened the door which has led to the synthesis of today's antibiotics. Although these "miracle drugs" have greatly reduced the mortality rate of many diseases, they may also cause a wide variety of adverse side effects. These reactions generally are mild, but at times have caused significant complications associated with antibiotic therapy--and even death. Some of the more common undesired reactions are pruritus, dizziness, rash, urticaria, fever, nausea, vomiting, blood dyscrasias, and abdominal discomfort. More serious reactions such as angioedema, exfoliative dermatitis, anaphylactic reactions, and intractable diarrhea may also result from antibiotic use (Goth 1976, p. 580).

Although diarrhea associated with antibiotic administration is not unusual (Fekety 1968, p. 210), considerable interest has been

focused on a "specific" type of colitis manifested by plaque-like elevations on the colonic mucosa that, on histologic examination, are found to be pseudomembranes (Tedesco et. al. 1974, p. 429). This type of colitis has been reported to develop in association with the use of various broad spectrum antibiotics. In recent years, the association of pseudomembranous colitis and patients receiving lincomycin and clindamycin has received increasing recognition. This colitis is usually a non-fatal illness, but it does require close supportive therapy, and by inference, follow-up care (Tedesco et. al. 1975, p. 481).

One of the unfortunate problems of today's medical therapy is that many non-acute patients do not receive follow-up care. Meeting patient needs should not be limited to their hospital stay, but should continue throughout their convalescence period. Advances in medical science has increased the chances for patient survival. As a result, there are a large number of patients who have "chronic diseases" for which continuous nursing services may be indicated.

The role of the clinical nurse specialist has been discussed throughout the literature. However, this role has been of a speculative nature and has never been rigorously explored. The clinical nurse specialist represents a new means for greatly improving the quality of both patient care and nursing practice (Georgopoulos and Christman 1970, p. 1030).

This study was undertaken to develop a tool which could be utilized by a clinical nurse specialist in the follow-up care of patients with antibiotic-induced pseudomembranous colitis.

Statement of the Problem

In this study, the following problems were examined:

1. What is the clinical course of antibiotic-induced pseudomembranous colitis, as found in the review of the literature?
2. What is the acute and post-acute course of antibiotic-induced pseudomembranous colitis, as found in the patients in the study institution?
3. Can a tool be developed from the information obtained that may be used by the clinical nurse specialist for the follow-up care of these patients?

Statement of the Purpose

The purposes of the study were:

1. To review all the pertinent literature regarding antibiotic-induced pseudomembranous colitis.
2. To review the chart of patients of pseudomembranous colitis in one study institution.
3. To categorize the findings from the literature with the findings from the cases reviewed in the study institution.

4. To compare the findings from the reviewed literature and the study institution.

5. To develop an assessment tool to be utilized by the clinical nurse specialist in follow-up care of patients with antibiotic-induced pseudomembranous colitis.

Background and Significance

Pseudomembranous colitis was first recognized in the 1800's and was thought to be an inflammatory reaction (Sleisinger and Fortran 1973, p. 1369). This type of colitis is a well documented, but poorly understood, inflammatory disease of the colon. The clinical disease is recognizable by the formation of membranous-like collections of exudate overlying the bowel mucosa. The etiology of this disease has yet to be defined. The wide variety of clinical circumstances in which antibiotic-induced pseudomembranous colitis occurs makes the search for its cause difficult. The majority of the reported cases exhibit underlying illnesses, surgery, and/or recent antibiotic therapy (Tedesco et.al. 1974, p. 429).

The severity of these cases varies widely (Viteri et. al. 1974, p. 1137). Mild forms of pseudomembranous colitis may be characterized by bloodless, watery diarrhea with fever, leukocytosis, and minimal proctoscopic and/or radiologic findings. However, the severe form of the disease is associated with marked abdominal pain, fever,

and leukocytosis. Proctoscopic and radiologic evidence of severe mucosal ulceration with pseudomembranes and possible pseudopolyp formation have been reported (Shapiro and Newman 1973, p. 263, Viteri et. al. 1974, p. 1137).

Drug induced colitis must be an important consideration in any patient who complains of fever, abdominal pain, or diarrhea and has recently received antibiotics. The clinical picture of this disease may also mimic an acute surgical emergency. Thus, a thorough history must be elicited from the patient. Antibiotic-induced pseudomembranous colitis can be self-limited when the diagnosis is made early and the offending drug is immediately discontinued (Tedsco et. al. 1974, p. 249). However, if the antibiotic is continued in the face of unsuspected pseudomembranous colitis, the diarrhea may be intractable and severe electrolyte disturbances will develop. With adequate supportive therapy the patient should recover completely (Tedesco et. al. 1975, p. 481).

Definition of Terms

For the purpose of this study, the following definitions were used:

1. Pseudomembranous colitis - "an inflammatory reaction affecting primarily the large bowel, but may also involve the small bowel. Grossly the bowel is dilated and has lost its usual mucosal

pattern. The mucosal surface is studded with raised yellow, whitish membranous plaques which in some areas may become confluent, giving the appearance of a membrane, hence its name" (Sleisinger and Fortran 1973, p. 1370).

2. Clinical nurse specialists - "are primarily nursing clinicians with a high degree of knowledge, skill, and competence in a specialized area of nursing. These are made directly available to the public through the provision of nursing care to clients and indirectly available through guidance and planning of care with other members of the health team. The clinical nurse specialist should hold a master's degree in nursing, preferably with an emphasis on clinical nursing" (American Nurse Association 1974).

3. Antibiotic - "a soluble substance derived from a mold or bacteria that inhibits the growth of other microorganisms" (Goodman and Gillman 1970, p. 1296).

4. Chloramphenicol - a "broad spectrum" antibiotic originally derived from Streptomyces venezuellae but presently synthetically produced. This antibiotic was introduced for usage in 1948, but by 1950 it was noted to produce serious and sometimes fatal blood dyscrasias. Chloramphenicol should be reserved for life threatening infections and is marketed in the United States under only the trade name Chloromycetin (Goodman and Gillman 1970, p. 1269).

5. Ampicillin - a widely used semisynthetic penicillin with "broad spectrum" antimicrobial efficacy. This antibiotic was introduced in the early 1960's and is presently available in the United States under a wide variety of trade names, including: Omnipen, Principen, and Polycillin (Goodman and Gillman 1970, p. 1223).

6. Tetracycline - a "broad spectrum" antibiotic prepared from the cultures of certain Streptomyces species. This bacteriostatic antibiotic has been available since the late 1940's and is presently available in the United States under such trade names as: Achromycin, Panmycin, Sumycin, and Terramycin (Goodman and Gillman 1970, p. 1253).

7. Lincomycin - an antibiotic first isolated from a soil sample from Lincoln, Nebraska as Streptomyces lincolnesis. The range of antibiotic activity in vitro and in vivo is similar to that of Erythromycin (Manashil and Kern 1973, p. 394, Lewis 1962, p. 570). The mechanism of action is by interference with bacterial protein synthesis. Lincomycin is marketed in the United States under only the trade name Lincocin (Goodman and Gillman 1970, p. 1296).

8. Clindamycin - a semisynthetic antibiotic which is the 7 chloro-7-deoxy modification of lincomycin (Cohen et. al. 1973, p. 1379, Butsch et. al. 1975, p. 152). Presently, the majority of usage

of this antibiotic is for the treatment of anaerobic infections. Clindamycin is available in the United States only under the trade name Cleocin (Howard 1973, p. 534).

Limitations

The limitations of this study were:

1. The age of the study population was limited to persons between eighteen and eighty years and with a confirmed proctoscopic diagnosis of antibiotic induced pseudomembranous colitis.
2. The study was limited to one investigator.
3. The study was limited to one hospital.
4. The records reviewed were limited to a time period between January 1970, when pseudomembranous colitis secondary to antibiotic usage was first clearly documented at the study institution and June 1977, when the present investigation was completed.

Delimitations

The delimitations of this study were:

1. The literature reviewed was in the English language.
2. The study was limited to patients with a diagnosis of antibiotic induced pseudomembranous colitis who had been evaluated at the study institution between January 1970 and June 1977.

Assumptions

The following assumptions were made:

1. It is appropriate for a clinical nurse specialist to follow non-acute patients.
2. The information contained in the medical records was accurate.

Summary

The twentieth century has brought many advances to the field of medicine, which have increased life expectancy by decreasing the morbidity and the mortality of certain life-threatening diseases. The broad-spectrum antibiotics have played a major role in the irradiation of many potentially lethal infectious diseases. However, they have also been incriminated as causative factors in potentially lethal adverse reactions. One of the most devastating of these adverse reactions is antibiotic-induced pseudomembranous colitis. This reaction has been reported with the administration of broad spectrum antibiotics.

The purposes of this study were to : review all of the pertinent literature regarding information about antibiotic-induced pseudomembranous colitis and correlate these findings with the findings from the cases reviewed at the study institution. The categorized findings from the literature and from the patients' records were

compared and the results formed the structure for the development of a nursing assessment tool. This tool was designed for use by the clinical nurse specialist to enhance the assessment, care, and education of patients with the diagnosis of antibiotic-induced pseudomembranous colitis.

Overview of the Following Chapters

A discussion of the past studies which have described patients with antibiotic-induced pseudomembranous colitis will be presented in Chapter II, "Review of the Literature." Chapter III entitled, "Procedure for Collection and Treatment of Data," describes: (1) the setting and the population for the study; (2) the criteria to be measured; (3) the procedure for collecting the data; and (4) the treatment methodology for the analysis of the data. Chapter IV, "Analysis of Data," is presented in a three part analysis including: (1) the categorization of the findings in the literature into overall percentage ratings; (2) categorization of the findings in the study institution, given in percentage ratings; and (3) a comparison of the two. Chapter V, "Summary, Conclusions, Implications, and Recommendations," will: (1) summarize the study; (2) present the conclusions and implications derived from the study; and (3) offer recommendations for further study.

CHAPTER II

REVIEW OF LITERATURE

Perhaps no other advance in medicine has had the impact on patient care as have the broad-spectrum antibiotics. These drugs have greatly decreased both the morbidity and mortality rates of many infectious diseases and the complications of countless other diseases. But, unfortunately, as with so many other drugs, the antibiotics often exhibit undesirable side effects. These side effects vary widely and rarely include diarrhea associated with pseudomembranous colitis. This reaction can be quite devastating to the patient if supportive therapy is not initiated promptly. Therefore, it is of the utmost importance that health providers be able to recognize not only the early signs and symptoms of antibiotic-induced colitis, but also the specific drugs associated with this disease.

The first cases of pseudomembranous colitis were apparently reported by Billroth in 1867 (Birnbaum et. al. 1961, p. 345, Jackson and Anders 1972, p. 154). Despite its recognition over 110 years ago, the etiology of this disease has remained a mystery, although, recently an animal model of the disease was reported in the

in the literature (Katz et. al. 1977, p. 1078). Many have postulated possible causative factors for pseudomembranous colitis, however, recently antibiotics have been increasingly incriminated (Birnbaum et.al. 1961, p. 345, Jackson and Anders 1973, p. 154, Manashil and Kern 1973, p. 394, Schapiro and Newman 1973, p. 263, Scott et. al. 1973, p. 1232, Hakkal 1974, p. 78, Davis 1974, p. 16, Berkowitz et. al. 1975, p. 362, Summer and Tedesco 1975, p. 237, Tedesco et. al. 1975, p. 481). Pseudomembranous colitis has been reported to occur spontaneously without any prior insult to the colonic mucosa (Pettet et. al. 1954, p. 546). The disease closely resembles the picture seen in the acute phase of chronic ulcerative colitis (Viteri et. al. 1974, p. 1137, Davis 1974, p. 16). Numerous clinical settings have been described in association with pseudomembranous colitis including: (1) postoperative states following colonic surgery (Schapiro and Newman 1974, p. 267, Summer and Tedesco 1975, p. 239, Tedesco et. al. 1975, p. 481), (2) colonic obstruction secondary to both intrinsic and extrinsic lesions (Goulston and McGovern 1965, p. 207), (3) generalized states of debility (Goulston and McGovern 1965, p. 207), and (4) ischemia due to decreased colonic blood supply (Tedesco et. al. 1974, p. 429, Butsch et. al. 1975, p. 152). With the introduction of broad-spectrum antibiotics reports of staphylococcal overgrowth as a causative factor for pseudomembranous colitis have been cited by some authors

(Birnbaum et. al. 1961, p. 345, Altemeier et. al. 1963, p. 847, Hakkal 1974, p. 81, Tedesco et. al. 1974, p. 429, Tedesco 1975, p. 481). Of the multiple causative factors for pseudomembranous colitis discussed in the literature, the broad-spectrum antibiotics are now the most frequently incriminated (Koltz et. al. 1953, p. 44, Goulston and McGovern 1965, p. 207, Cohen et. al. 1973, p. 1379, Scott et. al. 1973, p. 1232, Tedesco et. al. 1974, p. 429, Pittman et. al. 1974, p. 368, Berkowitz et. al. 1975, p. 362, Tedesco et. al. 1975, p. 481, Theodoropoulos et. al. 1975, p. 435). Initially, the broad spectrum antibiotics, such as tetracycline (Koltz et.al.1953, p. 44) and chloramphenicol (Reiner et. al. 1953, p. 39) were incriminated as causative agents. More recently the antibiotics used to treat anaerobic infections have been proven to have a causative role in the etiology of this disease (Davis 1975, p. 16). The two major anaerobic spectrum antibiotics to be incriminated are lincomycin (Lincocin) and clindamycin (Cleocin) (Davis 1975, p. 16, Tedesco et. al. 1974, p. 429, Theodoropoulos et.al. 1975, p. 435, Tedesco et. al. 1975, p. 481).

Antibiotic-induced pseudomembranous colitis has been reported to be four times more frequent in women than in men. The reported cases have been suggested to fall into two age categories, a younger group being under thirty years of age and an elderly group over fifty-five years of age (Ramirez-Ronda 1974, p. 860).

When used with discretion, most antibacterial agents are relatively free from significant side effects. If given by mouth, most antibiotics have the ability to cause mild gastrointestinal dysfunction, of which loose stools are the most common manifestation (Fekety 1968, p. 144). However, intractable diarrhea has been seen in patients even after only a few doses of the offending antibiotic (Fekety 1968, p. 145).

In the following sections, the various antibiotic agents which may produce pseudomembranous colitis are reviewed. Next, the clinical features of this disease entity are described. Finally, the role of the nurse clinical specialist is discussed.

Antibiotics as Causative Agents in Pseudomembranous Colitis

Chloramphenicol

The earliest description of antibiotic induced pseudomembranous colitis is by Reiner et. al. (1952, p. 39) who described several cases of pseudomembranous colitis associated with chloramphenicol and tetracycline. Due to its possible lethal side effects, chloramphenicol should not be used for trivial infections. Rather, it should be reserved for situations in which susceptible organisms are not affected by less potentially dangerous drugs. However, it must be noted that in life-threatening, overwhelming infections of doubtful etiology, the wide spectrum of activity makes chloramphenicol a valuable drug (Howard 1973, p. 551).

Pseudomembranous colitis is but one of many adverse reactions arising from the use of chloramphenicol. Other severe adverse reactions include blood dyscrasias (including aplastic anemia), allergic reactions (i.e., rashes, angioneurotic edema, urticaria), and "gray syndrome" in infants (Goth 1976, p. 591). Along with the multiple adverse reactions of chloramphenicol, therapeutic doses of this drug may interfere with the activity of other drugs. Therapeutic doses of chloramphenicol may inhibit the biotransformation of Orinase, Dilantin, Dicumarol and other drugs metabolized by the liver microsomal enzymes (Howard 1973, p. 552).

Several cases of pseudomembranous colitis confined to the colon were described. Grossly, the colons of patients with chloramphenicol-induced pseudomembranous colitis exhibited diffuse mucosal involvement with multiple confluent yellowish plaques, ranging from 0.1 cm to 0.6 cm in size. Microscopically, these plaques revealed cellular infiltration and inflammation consistent with pseudomembranes.

Ampicillin

Ampicillin, a semisynthetic penicillin was originally introduced to broaden the spectrum of activity of Penicillin-G to include many gram negative bacteria (Howard 1973, p. 514). Hypersensitivity reactions such as pruritis, rash, urticaria, eosinophilia, fever, and

angioedema are the most commonly observed ampicillin side effects (Howard 1973, p. 55). Diarrhea, resulting from an alteration in the intestinal flora, is also a common side effect (Berkowitz et. al. 1975, p. 36).

Pseudomembranous colitis has been observed during or immediately after ampicillin therapy and the importance of early diagnosis and adequate treatment in this disease has been stressed by Berkowitz and co-workers (1975, p. 362). In their cases, the patients had received ampicillin for a wide variety of conditions. Proctoscopic examinations revealed the classic findings of yellow-white plaques which averaged 2 mm to 2 cm in size. Microscopic examination confirmed that the pseudomembranes were composed of mucus and neutrophils erupting from the mucus glands which were distended with a thickened zone of fibrin exudate.

Tetracycline

The broad spectrum antibiotic, tetracycline, also causes pseudomembranous colitis (Koltz et. al. 1953, p. 44, Reiner et. al. 1952, p. 39). As with the other antibiotics, the onset of symptoms usually developed five to six days after the initiation of therapy. Although tetracycline may cause multiple adverse reactions, gastrointestinal effects are the most common. These range from anorexia, to nausea, vomiting, or diarrhea. Pseudomembranous colitis may

result from either oral or parenteral administration of tetracycline (Koltz et. al. 1953, p. 44). Proctoscopic findings in these studies were compatible with pseudomembranous colitis.

Lincomycin and Clindamycin

Of all the broad-spectrum antibiotics, lincomycin and its derivative clindamycin have probably caused more cases of pseudomembranous colitis than all the other antibiotics combined. The mechanism or mechanisms by which these drugs cause diarrhea are not, as yet, fully documented. However, recently several potential mechanisms have been postulated. These include: (1) alteration of the normal intestinal flora by the antibiotic with subsequent resistant bacterial overgrowth (Scott et. al. 1973, p. 1232), (2) poor absorption of the antibiotic in the small bowel (Davis 1975, p. 16), and (3) the possible irritant effects antibiotic metabolites on the colonic mucosa (Manashil et. al. 1973, p. 394, Pittman et. al. 1974, p. 368). These antibiotic metabolites were recovered from the stool and are postulated to be absorbed by the columnar epithelial cells of the bowel. Within the epithelial cells of the colonic mucosa it is postulated that ribosomal function, and thus protein synthesis is altered. This disruption of protein synthesis is the documented mechanism of action of clindamycin

on susceptible bacteria (Schapiro and Newman 1973, p. 397, Pittman et. al. 1974, p. 368, Butsch et. al. 1975, p. 152).

Lincomycin was first introduced as a broad-spectrum antibiotic in 1962. Since that time, there have been several reports of colitis developing in patients who were taking this drug (Pittman et. al. 1973, p. 368, Manashil and Kern 1973, p. 394, Scott et. al. 1973, p. 1232, Davis 1974, p. 16). It has been reported by Kaplan and Weinstein (1968, p. 131) that an oral dose of lincomycin is better absorbed from the gastrointestinal tract when the patient is in the fasting state. Intestinal absorption may be reduced up to 50 percent when administration is closely followed by a meal, thus allowing approximately one-half of the unabsorbed dose to reach the colon (Kaplan and Weinstein 1968, p. 131). Lincomycin causes diarrhea in about 20 percent of patients to whom this drug is administered (Goodman and Gilman 1970, p. 1297).

Due to the poor absorption of lincomycin and its gastrointestinal side effects, in 1968 clindamycin was introduced (Cohen et.al. 1973, p. 1379, Theodoropoulos et. al. 1975, p. 435). This semi-synthetic lincomycin derivative is five to eight times more potent than lincomycin against most gram-positive organisms (Geddes et. al. 1970, p. 703). Although clindamycin was initially reported to be better absorbed by the gastrointestinal tract than lincomycin, recent reports

have shown that it is a significant cause of pseudomembranous colitis (Cohen et. al. 1973, p. 1379, Tedesco et. al. 1974, p. 429, Viteri et. al. 1974, p. 1137, Butsch et. al. 1975, p. 152, Theodoropoulos et. al. 1975, p. 435, Summer and Tedesco 1975, p. 237, Tedesco et. al. 1975, p. 481, Goodacre et. al. 1977, p. 149). As in other instances of antibiotic-induced pseudomembranous colitis, the initial clinical symptoms include abdominal pain, nausea, and anoxeria with intractible diarrhea (Cohen et. al. 1973, p. 1279, Shapiro and Newman 1973, p. 263, Tedesco et. al. 1975, p. 481). Like lincomycin, the mechanisms of clindamycin-induced pseudomembranous colitis remains an enigma.

Clindamycin has the same therapeutic indications as does its parent drug, lincomycin. Clindamycin may be administered orally, intramuscularly or intravenously. Initially, gastrointestinal side effects were reported to be a rare adverse reaction (Wagner et. al. 1968, p. 25). However, Tedesco and co-workers (1974, p. 429) reported that 21 percent of their clindamycin treated patients developed diarrhea, and 10 percent developed pseudomembranous colitis.

Thus within the past twenty-five years, a causal relationship between the use of certain broad spectrum antibiotics and the development of pseudomembranous colitis has been established. The incidence of this rare adverse reaction increased dramatically, however, after

the introduction of lincomycin and its semisynthetic derivative clindamycin (Cohen et. al. 1973, p. 1374, Tedesco et. al. 1974, p. 429, Tedesco et. al. 1975, p. 481, Summers and Tedesco 1975, p. 237).

Clinical features

The subjective symptoms of antibiotic induced pseudomembranous colitis are usually vague and non-specific. These symptoms commonly include lower abdominal cramping, hypogastric pain and elevation of temperature, usually not exceeding 102°F (Cohen et. al. 1973, p. 137, Tedesco et. al. 1975, p. 481). The objective findings of this syndrome may mimic either ulcerative colitis or an acute surgical abdomen. The onset of clinical symptoms is usually abrupt and may occur at any time from a few days to several weeks after administration of the offending antibiotic. The severity of the illness varies from that of bloodless, watery diarrhea without other constitutional symptoms to severe forms accompanied by elevation of temperature, bloody diarrhea, and marked leukocytosis (Davis 1975, p. 16, Viteri et. al. 1974, p. 1137, Tedesco et. al. 1975, p. 481). The clinical course may end just as abruptly as it began or it may be protracted. The average duration of symptoms is reported to be approximately five weeks (Viteri et. al. 1974, p. 1137, Tedesco et. al. 1975, p. 481).

Laboratory data

Pseudomembranous colitis associated with antibiotic therapy is being reported with increased frequency. The use of laboratory data to document the progress of the illness has so far been futile (Tedesco et. al. 1974, p. 429). However, with severe diarrhea there may be a electrolyte disturbance and/or hypoalbuminemia. Leukocytosis is often the only abnormal hematologic value and may vary from 9000 to 37,500 white blood cells per cubic millimeter (Schapiro and Newman 1973, p. 263, Tedesco et. al. 1975, p. 481, Berkowitz et. al. 1975, p. 362). Various degrees of anemia, which appear to be the result of moderate to severe bloody diarrhea, have been reported in some studies (Birnbaum et.al. 1961, p. 345, Slesinger and Fortran 1973, p. 1370). Also immunoelectrophoretic pattern changes in both urine and serum have appeared in a few cases (Butsch et. al. 1975, p. 152). Dramatic increases in both the serum glutamic oxaloacetic transaminase (SGOT) and alkaline phosphatase have also been reported in some cases (Butsch et. al. 1975, p. 152, Tedesco et. al. 1975, p. 481). However, these alterations occur so infrequently that significant data has not been collected to correlate these findings with the disease (Butsch et. al. 1975, p. 152).

Roentgenologic studies have proven to be both beneficial, if positive, but an obstacle, if negative in establishing the diagnosis of pseudomembranous colitis as noted later in the study. The most common radiographic findings are: (1) ulcerations, (2) shaggy edematous mucosa, and (3) excessive mucus secretion (Theodoropoulos et. al. 1975, p. 435, Hakkal 1975, p. 78). Although these findings cannot differentiate between pseudomembranous colitis and other inflammatory bowel diseases, antibiotic-induced colitis should be a strong diagnostic consideration whenever there is a clinical history of recent antibiotic therapy (Manashil and Kern 1972, p. 394, Cohen et. al. 1973, p. 1379, Tedesco et. al. 1974, p. 481, Tedesco et. al. 1975, p. 481).

The barium examination of the colon should be done only after an adequate proctoscopic examination has been performed. This order allows determination of the extent of bowel involvement. If, however, the barium enema is performed prior to proctoscopy, the proctologist's view is usually greatly compromised by retained barium and thus a true picture of the mucosal involvement cannot be appreciated. This is due to the irritant effect of the barium on the mucosal lining (Briggs 1977).

The proctoscopic examination is the single most important diagnostic test for pseudomembranous colitis. The major findings are raised, plaque-like pseudomembranes, erythema, and edema with

friability and granularity (Cohen et. al. 1973, p. 1377, Tedesco et. al. 1974, p. 429, Tedesco et. al. 1975, p. 481). When rectal biopsies are obtained, they demonstrate marked mucosal inflammation, which is predominately neutrophilic in cell type (Cohen et. al. 1973, p. 1379, Tedesco et. al. 1974, p. 429, Tedesco et. al. 1975, p. 481). Cultures obtained at the time of the proctoscopic exams have been reported to be negative (Pittman et. al. 1974, p. 368, Davis 1975, p. 16, Berkowitz et. al. 1975, p. 362).

Therapy

Therapy for antibiotic-induced pseudomembranous colitis has consisted of supportive care including nasogastric suction, intravenous fluids, and antidiarrheal drugs. The usefulness of antidiarrheal agents is highly debatable in the treatment of this disease (Ramirez-Ronda 1974, p. 860, Goodacre et. al. 1977, p. 149). Various forms of steroid therapy have also been employed in the treatment of this illness. Oral steroid therapy and the rectal administration of steroids, by enema or suppository, have been utilized. However, these therapeutic treatment modalities do not appear to modify the course of the disease (Viteri et. al. 1974, p. 1137), although isolated instances of dramatic improvement have been reported (Pittman et. al. 1974, p. 368). In one case report, an endogenous increase in cortisol by the administration

of adrenocorticotrophic hormone (ACTH) was reported as successful in relieving the diarrhea (Schapiro and Newman 1973, p. 263). The most important initial aspect of therapy is the imperative necessity for the immediate discontinuation of the offending antibiotic. It has been shown that in patients in whom the diagnosis was either delayed or overlooked, and antibiotic therapy was continued, the course of the disease was more prolonged and severe (Tedesco et. al. 1975, p. 481, Davis 1975, p. 16, Berkowitz et. al. 1975, p. 362). These patients also had a tendency to more frequently develop electrolyte imbalances and/or hypoalbuminemia (Groll et. al. 1970, p. 88, Tedesco et. al. 1974, p. 429, Tedesco et.al. 1975, p. 481).

The nursing management of patients with antibiotic-induced pseudomembranous colitis involves meeting the patient's physical, psychological, and social needs. Very little has been written in regard to the nursing care of the patient with diarrhea secondary to antibiotic therapy. However, due to the potential hazards of this disease, the nurse must not only provide immediate care, but must also be ready to participate in the patient's long term care. But unfortunately, both the medical and nursing literature has failed to provide information on the follow-up assessment of these patients.

Clinical Nurse Specialist

The clinical nurse specialist has been described as a counterpart of the clinician in medicine (Reiter 1966, p. 276). As a member of a team with a voice in responsibilities for the patient's care, clinical nurse specialists must command an expertise in their specific area of interest. The clinical nurse specialist is a member of the health team through which guidance and counselling provides primary care. To be able to function within this role, the clinical nurse specialists must be willing to be accountable for their actions, be decision makers and be well versed in communicative problem solving, and refined technical skills (Reihl 1973, p. 100).

There have been many roles developed or identified for the clinical nurse specialist. They include practitioner, consultant, teacher, counselor, coordinator, and researcher (Reihl 1973, p. 17). In order to wear these many hats, clinical nurse specialists must be able to apply their acquired knowledge to specific patient problems. This requires an advanced knowledge of pathophysiology, pharmacology, and the psychological aspects of the illness. Of the three commitments identified by Berlinger (1973, p. 104) the commitment of assisting others to attain their optimum level of wellness must be considered foremost. However, the other commitments must also be recognized in

order to develop the role of the clinical nurse specialist. These include continual advancement of nursing education and the belief of independent but collaborative clinical practice.

Today, the practice of nursing and nursing education are going through the most stressful time of their professional "life". Throughout a long and turbulent history, nursing has faced almost insurmountable difficulties. Over the past century, nursing has evolved from care of the sick person in the hospital, to the concern for his restoration, to maintenance of health. Thus the classical role of the nurse has expanded beyond the walls of the hospital. The clinical nurse specialist's practice has extended into the community in the form of caring for families in the clinics, at work, and in the home. Therefore, nursing today is moving into a new, enlarged, and ever more crucial role in health care delivery (Aradine and Denyes 1973, p. 411).

Clinical practice is the center of nursing. The clinical nurse specialist serves as a model of expertness representing advanced and newly developing practices to the staff nurse (Georgopoulos and Christman 1970, p. 1030). Theoretically, the clinical nurse specialist not only works with the most complex problems in nursing, but also through such work provides literature which helps constantly to revise

the general practice of nursing (Aradine and Denyes 1972, p. 411).

The clinical nurse specialist also develops innovated ideas based on emerging new knowledge.

There is a mounting interest in utilization of the clinical nurse specialist in both the hospital setting and in the out-patient clinic. The interest may be in response to the ever growing need to personalize patient care in an age of science and technology (Thomstad 1974, p. 1993). There are three considerations that must be understood in order to better utilize the clinically prepared nurse specialist. These are: (1) methods of assigning these nurses must allow them a degree of freedom in the organizing of nursing care; (2) their caseload must be limited in order to allow them to have close personal contact with their patients, and (3) new methods for recognition must be developed so that the competent clinical specialist may practice primary care without being "promoted" out of their practice (Skully 1965, p. 28).

The clinical nurse specialist in the clinic, hospital, or community setting, and the staff nurse in the hospital should be made aware of the prevalence of antibiotic-induced pseudomembranous colitis and its manifestations. They must also be aware of the electrolyte and fluid imbalances that may accompany this disease (Groll et. al. 1970, p. 88, Cohen et. al. 1973, p. 1379, Tedesco et. al. 1975, p. 481). The nurse must be able to recognize the physical signs and symptoms of this

colitis and be able to interpret the positive laboratory findings that are characteristic with this illness. An in-depth knowledge regarding the most common of the offending drugs which may cause pseudomembranous colitis is essential.

Summary

Antibiotic-induced pseudomembranous colitis is an adverse reaction resulting from many potential causative factors. The most common of these factors is the broad-spectrum antibiotics. The disease is self-limited when the diagnosis is made early and when prompt supportive therapy is initiated. However, if the disease is unsuspected, there may be severe problems of electrolyte disturbances and the development of hypoalbuminemia. Patients who progress to this stage of the disease usually have a high morbidity rate and occasionally death may result. While a mild anemia, increased leukocyte count, or elevated alkaline phosphatase or SGOT may accompany the disease, only the proctoscopic examination coupled with the appropriate history is diagnostic. Since most subjective and objective findings are vague and non-specific, diagnosis of pseudomembranous colitis may be easily overlooked. Drug induced colitis must be an important consideration in any patient who has recently received antibiotics and develops fever, abdominal pain and diarrhea.

The twentieth century has brought many advances in the field of medicine and nursing. One of the foremost contributions has been the development of the broad-spectrum antibiotics. Unfortunately, the indiscriminate use of these powerful drugs for trivial infections has led to many adverse reactions. In today's hospital scene, the nurse is a major provider of patient care and therefore it is the nurse who often identifies numerous initial patient problems. Therefore, the nurse must be acutely aware of specific signs and symptoms of drug reactions.

The nursing profession must also acknowledge that patient care is not limited to the hospital setting and to an eight hour shift. Patient care is a twenty-four hour a day undertaking. Long term care of the patient must be the responsibility of not only the physician, but also of the nurse. Thus the clinical nurse specialist should be an intricate part of the follow-up care of the patient. Advanced knowledge and skills are used in the planning of adequate long-term care. It is the clinical nurse specialist who may be instrumental in insuring care for the post-acute patient. It is recognized that knowledge of the symptoms of an impending disease aids in its early detection. One such disease is antibiotic-induced pseudomembranous colitis.

CHAPTER III

PROCEDURE FOR COLLECTION AND TREATMENT OF DATA

The methodology employed in this study was that of an analytical review of the literature and the medical records of persons with a diagnosis of antibiotic induced pseudomembranous colitis at the study hospital. All medical records were thoroughly read by the investigator and measured against previously established criteria (taken from the literature), as well as those suggested by an expert panel (see Appendix B). The panel consisted of four gastroenterologists and four nurses with previous interest in this area.

Setting

The study was conducted in a small private office in the Gastroenterology Department of Scott and White Memorial Hospital and Clinic, Temple, Texas. This is a large diagnostic center that has a bed capacity of approximately five hundred. Many of the patients seen in this center are referred from their local physicians within the surrounding counties. However, approximately an equal number come from throughout the state of Texas, several of the states throughout the country, and Mexico. The yearly patient visits average over a quarter

of a million at the study institution. There is a permanent senior staff of over one hundred and twenty physicians and a housestaff of over eighty resident physicians.

Population

The population of the study consisted of all patients with a final diagnosis of antibiotic-induced pseudomembranous colitis who were seen from January 1970 when this disease entity was clearly documented at the study institution, through June 1977. Nineteen of the twenty-seven potential patients indentified by discharge code numbers fulfilled the criteria of antibiotic usage and proctoscopic documentation of pseudo-membranes and were therefore included in the study.

Tool

To analyze the data obtained from the medical records of persons identified with documented pseudomembranous colitis, a list of specific variables (i.e., symptoms, duration of illness, complications, etc.), to be measured was established from the literature reviewed and then broadened by the expert panel (see Appendix B.).

Collection and Treatment of Data

Before the study was implemented, permission was obtained from the Assistant Administrator of Nursing Service and the Chief of the

Section of Gastroenterology at the study hospital (see Appendix A.). Because the institution is a teaching and research center, all patients entering the clinic or the hospital routinely sign a release form allowing information contained in the medical records to be used for research purposes. All cases were individually reviewed and the pertinent information was recorded on all variables to be studied, if that information was contained in the medical record.

The values for each of the listed variables were tabulated to obtain a mean from the medical records studied and from the previous studies reviewed in the literature. The averages were then compared, by percentages, in order to determine if the analyzed variables from the study institution correlated with the previously published reports. The findings from this study have been used to formulate an assessment tool to be utilized by the clinical nurse specialist in the long-term care of patients with antibiotic induced pseudomembranous colitis. This information may also be beneficial for patient, family and staff education programs on antibiotic-induced pseudomembranous colitis.

Summary

A critical analysis of the pertinent literature regarding antibiotic-induced pseudomembranous colitis was accomplished and was categorized into percentage ratings. The study was implemented in a

large diagnostic center in which multiple physician referrals are evaluated yearly. The medical records of nineteen persons with a final diagnosis of antibiotic-induced pseudomembranous colitis were reviewed and the data obtained was compared with a list of variables drawn from the studies reviewed in the literature. Mean values for each of the variables were tabulated and compared by percentage. From the values an assessment tool was developed.

The following chapter presents the analysis of the data collected.

CHAPTER IV

ANALYSIS OF DATA

Reports of antibiotic-induced pseudomembranous colitis have been increasing in the literature with the increased reliance upon these drugs and the variety of antibiotics available. Several broad-spectrum antibiotics have now been incriminated as causative agents in this disease entity. In this chapter, a three part analysis of the previously defined variables will be presented: (1) the compiled review of the studies from the literature; (2) the data obtained from the study hospital; and (3) a comparison of the two. To provide continuity within the presentation of the compiled data, the three component parts of the study will be described in a combined fashion, although each component was completed before the next was begun.

Incidence

The incidence of antibiotic-induced pseudomembranous colitis in the literature has been reported to be 10 percent in a single prospective study (Tedesco et. al. 1974, p. 249). Due to the retrospective nature of the present study, the incidence of this disease at the study hospital could not be obtained with accuracy, as it was unclear

whether the diagnosis of antibiotic-induced pseudomembranous colitis was listed in the final discharge summary of all patients who actually had the disease.

Although very little has been reported with respect to the racial incidence of antibiotic-induced pseudomembranous colitis, both age and sex of patients with this disease has been frequently reported (table 1).

Two studies have noted a female predominance in this disease (Tedesco et. al. 1974, p. 429, Ramirez-Ronda, 1974, p. 860). Other published reports, however, do not appear to substantiate this finding (see table 1). The total ratio, compiled from the literature does, however, show a modest female predominance. In the study institution, females were afflicted with antibiotic-induced pseudomembranous colitis almost twice as frequently as were males (table 2), thus supporting the female predominance reported by Tedesco and co-workers (1974, p. 429) and Ramirez-Ronda (1974, p. 860).

Two distinct age groups of patients with antibiotic-induced pseudomembranous colitis were identified by one author (Ramirez-Ronda 1974, p. 860); a younger group under thirty years of age and an older group over fifty-five years of age. The computed mean age of the patients reported in the literature was forty-nine years old. The finding of two distinct groupings does not appear to be supported by other

TABLE 1

AGE, SEX, AND RACIAL DISTRIBUTION OF CASES WITH
ANTIBIOTIC-INDUCED PSEUDOMEMBRANOUS
COLITIS FROM LITERATURE REVIEWED

STUDY	YEAR	NUMBER OF CASES STUDIED	MEAN AGE	SEX MALE:FEMALE	RACE WHITE:BLACK
Koltz et. al.	1953	5	45.4	3: 2	4:0
Cohen et. al.	1973	3	50.3	1: 2	3:0
Manashil and Kern	1973	3	33	0: 3	3:0
Pittman et. al.	1973	16	55.5	9: 7	16:0
Schapiro and Newman	1973	4	47.5	1: 3	--
Scott et. al.	1973	8	55.5	6: 2	--
Davis	1974	4	54.1	3: 1	--
Hakkal	1974	2	34.5	0: 2	--
Tedesco et. al.	1974	20	51	6:14	15:5
Viteri et. al.	1974	7	59	3: 4	7:0
Berkowitz et. al.	1975	1	37	1: 0	0:1

TABLE 1
Age, Sex, and Racial Distribution of Cases With
Antibiotic-Induced Pseudomembranous
Colitis From Literature Reviewed (continued)

STUDY	YEAR	NUMBER OF CASES STUDIED	MEAN AGE	SEX MALE:FEMALE	RACE WHITE:BLACK
Butsch et. al.	1975	1	79	1: 0	1:0
Summer and Tedesco	1975	23	52	7:16	--
Theodoropolus et. al.	1975	1	38	1: 0	--
Goodacre et. al.	1977	2	48.5	0: 2	--
TOTAL		100	49.35	.72: 1	8.16:1*

*May be dependent upon client population.

TABLE 2

AGE AND SEX OF CASES WITH ANTIBIOTIC-INDUCED
PSEUDOMEMBRANOUS COLITIS IN STUDY HOSPITAL
JANUARY 1970 - JUNE 1977

AGE	MALES	FEMALES	TOTAL
20-29	--	1	1
30-39	--	2	2
40-49	2	--	2
50-59	--	2	2
60-69	4	6	10
70-79	1	1	2
80-89	--	--	0
TOTAL	7	12	19

studies in the literature in which patient ages were cited and is not confirmed by the age distribution in the study institution in which over one-half of the cases were clustered between ages sixty to sixty-nine. (table 2).

Only two studies in the reviewed literature noted antibiotic-induced pseudomembranous colitis in non-white patients (Tedesco et. al. 1974, p. 429, Berkowitz 1975, p. 362). Only six of the fifty-two total

patients reported in the literature were non-white, yielding a non-white incidence of one to nine. No non-white patients were noted to have developed this disease in the patients reviewed in the study hospital.

Causative Antibiotic Agents

Although reports of non-antibiotic associated pseudomembranous colitis have appeared in the literature (Golston and McGovern 1965, p. 207), certain broad spectrum antibiotics now represent the major causative factor in this disease. The most frequently incriminated antibiotics are chloramphenicol, ampicillin, tetracycline, lincomycin, and clindamycin. From the compiled data of the literature review, lincomycin and clindamycin account for approximately three-fourth of all the reported cases (table 3).

Various studies have described the duration of antibiotic therapy prior to the onset of diarrhea. In a few of the case reports, the antibiotic was even continued in spite of obvious diarrhea and previous reports in the literature incriminating the offending antibiotic (Pittman et. al. 1973, p. 368, Schapiro and Newman 1973, p. 263, Tedesco et. al. 1974, p. 429, Butsch et. al. 1975, p. 152, Goodacre et. al. 1977, p. 149). The period of time from the discontinuation of, or the completion of, antibiotic therapy to the subsequent diagnosis of pseudomembranous colitis varied from two days to one month, but

TABLE 3

ANTIBIOTIC CAUSATIVE AGENTS OF CASES WITH ANTIBIOTIC-
INDUCED PSEUDOMEMBRANOUS COLITIS
FROM LITERATURE REVIEWED

STUDY	YEAR	NUMBER OF CASE STUDIES	CHLORAM- PHENICOL	AMPI- CILLIN	TETRA- CYCLINE	LINCO- MYCIN	CLINDA- MYCIN	
Riener et. al.	1952	7	1	--	6	--	--	
Koltz et. al.	1953	5	--	--	5	--	--	
Cohen et. al.	1973	3	--	--	--	--	3	
Pittman et. al.	1973	16	--	--	--	16	--	40
Schapiro and Newman	1973	4	--	1	1	2	--	
Scott et. al.	1973	8	--	--	7	--	--	
Davis	1974	4	--	--	--	2	2	
Hakkal	1974	2	--	1	--	--	1	
Tedesco et. al.	1974	20	--	1	--	--	14	
Viteri et. al.	1974	7	--	--	--	4	3	

TABLE 3
Antibiotic Causative Agents of Cases With Antibiotic -
Induced Pseudomembranous Colitis
From Literature Reviewed (continued)

STUDY	YEAR	NUMBER OF CASE STUDIES	CHLORAM- PHENICOL	AMPI- CILLIN	TETRA- CYCLINE	TETRA- MYCIN	CLINDA- MYCIN
Summer and Tedesco	1975	23	--	--	--	--	23
Tedesco et. al.	1975	8	--	--	--	2*	8
TOTALS		107	7	3	19	26	54

*Lincomycin administered concomittantly with clindamycin.

averaged approximately one week (Pittman et. al. 1973, p. 368, Viteri et. al. 1974, p. 1137). In three cases the antibiotic was continued for two, four, and eight days despite the development of significant diarrhea (Schapiro and Newman 1974, p. 263, Cohen et. al. 1973, p. 1379, Butsch et. al. 1974, p. 152). In one case reported by Goodacre and co-workers (1977, p. 149), a woman reported having diarrhea which continued for six months after receiving clindamycin but was administered this antibiotic again. This resulted in a worsening of the diarrhea to the point that large quantities of mucous with flecks of blood were being passed rectally. Eventually, this patient required a subtotal colectomy and ileostomy with subsequent removal of the rectal stump.

In the study hospital, ampicillin, lincomycin, and clindamycin accounted for all but one of the reported cases of antibiotic-induced pseudomembranous colitis (table 4). The average duration of antibiotic therapy was ten days compared to eight days in the reviewed literature (table 4). In one case a patient was reported to have had a similar reaction four years prior to receiving the present antibiotic administration (table 4).

Thus the findings from the reviewed literature revealed that lincomycin and its derivative clindamycin were noted to cause pseudomembranous colitis in about 75 percent of the reported cases. From the present study, these two antibiotics were noted to be the causative

TABLE 4

ANTIBIOTIC CAUSATIVE AGENTS OF CASES WITH ANTIBIOTIC-
INDUCED PSEUDOMEMBRANOUS COLITIS IN STUDY HOSPITAL
JANUARY 1970 - JUNE 1977

Days From Initiation of Antibiotic to Onset of Symptoms
(Days of Total Antibiotic Administration)

CASE NO.	AMPI- CILLIN	TETRA- CYCLINE	LINCO- MYCIN	CLINDA- MYCIN
1	-	-	7 (7)	-
2	-	-	-	10 (7)
3	10 (7)	-	-	-
4	-	-	-	1 (1)
5	2 (2)	-	-	-
6	-	10 (14)	-	-
7	-	-	8 (5)	-
8	-	-	1 (1)	-
9	-	-	-	8 (7)
10	-	-	-	18 (7)*
11	3 (7)	-	-	-
12	-	-	-	14 (10)
13	2 (2)	-	-	-
14	-	-	-	9 (9)
15	-	-	14 (10)	-

TABLE 4
 Antibiotic Causative Agents of Cases with Antibiotic-
 Induced Pseudomembranous Colitis in Study Hospital
 January 1970 - June 1977 (continued)

CASE NO.	AMPI- CILLIN	TETRA- CYCLINE	LINCO- MYCIN	CLINDA- MYCIN
16	-	-	9 (12)	-
17	3 (7)	-	-	-
18	-	-	10 (7)	-
19	-	-	14 (5)	-
TOTAL	20 (25)	10 (14)	63 (46)	60 (41)

*Similar reaction to Lincomycin four years earlier.

factor in approximately 68 percent of the reviewed records. Thus, there was no significant difference between this study and the previous studies.

Chief Complaint and Clinical Manifestations

The reviewed literature revealed that the initial manifestations of antibiotic-induced pseudomembranous colitis were diarrhea and abdominal pain. As reported in the literature, the subjective symptoms were commonly non-specific. These included vague complaints of diffuse abdominal cramping which was often associated with fever, seldomly exceeding 102°F (Tedesco et. al. 1974, p. 429). The disease manifested itself as diarrhea and either resulted in the discontinuation of the antibiotic or began within five to seven days after the completion of antibiotic therapy (Summer and Tedesco 1975, p. 237).

In the study hospital, the initial complaints of all the patients was that of diarrhea which was chronic or recurrent and was unresolved after a period of initial therapy outside the study hospital. Of the referred cases over one-half had been previously treated without symptomatic improvement.

From the reviewed literature, diarrhea was the most striking feature in all the cases reported. The average duration of this diarrhea was reported to be two weeks (Pittman et. al. 1973, p. 364).

Abdominal pain was noted in 93 percent of the patients making it the next most significant finding in the reviewed literature (table 5). The abdominal pain varied widely in intensity and character from mild and diffuse to severe pain which warranted the consideration of possible surgical intervention (Tedesco et. al. 1975, p. 481). In the majority of the reported cases, the pain was characterized as diffuse and cramping, without radiation or specific localization. Fever was noted in 46 percent of the reported cases from the literature (table 5). The fever ranged from mild elevations to 104°F. Both the abdominal pain and the fever were noted to either precede or coincide with the onset of the diarrhea (Tedesco et. al. 1974, p. 429). The average duration of time for the complete resolution of clinical symptoms was six weeks (table 5).

In the study hospital, 84 percent of the reported cases had some type of abdominal pain (table 6). As noted in the literature, this pain was usually of a vague and generalized cramping nature, which did not localize or radiate to other parts of the body. Fever was noted in 53 percent of the study population (table 6). This also corresponded with the reports from the literature and ranged from 99.2°F to 103.6°F with an average of 101.6°F. However, it should be noted that almost one-half of the study population did not present with any elevation in temperature (table 6).

TABLE 5

CLINICAL FEATURES OF CASES WITH ANTIBIOTIC-
INDUCED PSEUDOMEMBRANOUS COLITIS IN
REVIEWED LITERATURE

STUDY	YEAR	NUMBER OF CASE STUDIES	AVERAGE MAX. NO. STOOLS/DAY	ABDOMINAL PAIN	FEVER	AVERAGE COMPLETE CLINICAL RESOLUTION IN WEEKS
Koltz et. al.	1953	5	10	5	3	18*
Cohen et. al.	1973	3	7	3	2	4
Schapiro and Newman	1973	4	11	3	2	4
Davis	1974	4	9	4	3	9
Hakkal	1974	2	--	2	2	4
Viteri et. al.	1974	7	10	4	6	5
Tedesco et. al.	1975	8	--	8	8	4
Summer and Tedesco	1975	23	--	23	--	2
Total number of Patients		56				
Average maximum number of stools/day			9			

TABLE 5
Clinical Features of Cases with Antibiotic -
Induced Pseudomembranous Colitis in
Reviewed Literature (continued)

STUDY	YEAR	NUMBER OF CASE STUDIES	AVERAGE MAX. NO. STOOLS/DAY	ABDOMINAL PAIN	FEVER	AVERAGE COMPLETE CLINICAL RESOLUTION IN WEEKS
Number of patients with clinical feature			56	52	26	
Percentage of patients with clinical feature			100	93	46	
Average weeks to complete resolution						6

*Includes one patient with disease duration of one year before being seen by reporting investigator.

TABLE 6

CLINICAL FEATURES OF CASES WITH ANTIBIOTIC-INDUCED
PSEUDOMEMBRANOUS COLITIS IN STUDY HOSPITAL
JANUARY 1970 - JUNE 1977

CASE NO.	AVERAGE MAX. NO. STOOLS/DAY	ABDOMINAL PAIN	FEVER	WEIGHT LOSS	AVERAGE COMPLETE CLINICAL RESOLUTION IN WEEKS
1	20	+	-	+	8
2	15	+	+	NR	2
3	7	+	+	+	4
4	NR	+	-	-	1
5	9	-	-	-	1
6	"Profuse"	-	-	-	2
7	"Copious"	+	+	-	4
8	9	+	-	+	5
9	5	+	-	+	5
10	6	+	+	+	2

TABLE 6
Clinical Features of Cases with Antibiotic-Induced
Pseudomembranous Colitis in Study
Hospital January 1970-June 1977 (continued)

CASE NO.	AVERAGE MAX. NO. STOOLS/DAY	ABDOMINAL PAIN	FEVER	WEIGHT LOSS	AVERAGE COMPLETE CLINICAL RESOLUTION IN WEEKS
11	17	+	-	NR	4
12	7	+	+	NR	2
13	6	+	-	+	3
14	12	+	+	+	4
15	12	+	+	+	3
16	6	+	-	+	2
17	15	+	+	+	2
18	20	+	+	+	2
19	3	-	+	NR	8
<hr/>					
Average Maximum Number of Stools/Day		11			

TABLE 6
Clinical Features of Cases with Antibiotic-Induced
Pseudomembranous Colitis in Study
Hospital January 1970-June 1977 (continued)

CASE NO.	AVERAGE MAX. NO. STOOLS/DAY	ABDOMINAL PAIN	FEVER	WEIGHT LOSS	AVERAGE COMPLETE CLINICAL RESOLUTION IN WEEKS
Number of Patients with Clinical Features		16	10	11	
Percent of Patients with Clinical Features		84	53	58	
Average Weeks to Complete Resolution					4

+ = positive finding
- = negative finding
NR = not recorded

The reviewed literature failed to report weight loss within their study populations. However, Koltz and co-workers (1953, p. 44), reported a case of a patient who had lost seventy to eighty pounds due to pseudomembranous colitis and was noted to have occurred over a six month period. In the study hospital, approximately 58 percent had weight loss.

The initial complaints and clinical findings in the reviewed literature and the study hospital were the same. In the literature, abdominal pain was noted to occur in 93 percent of the cases, compared to 84 percent of the study hospital cases. Fever in the literature was noted in 46 percent of the population reviewed. This compared to 53 percent from the study hospital. Only one case reported weight loss in the literature as noted earlier in the study and therefore was not included in the table. However, a significant number, 58 percent of the study hospital cases were noted to have weight loss.

Previous Bowel History

Only three studies have reported on the previous bowel history of patients who developed antibiotic-induced pseudomembranous colitis (Pittman et. al. 1973, p. 368; Tedesco et. al. 1974, p. 429; Davis 1974, p.16). In all sixteen of the patients reported by Pittman and co-workers (1973, p. 368), none had a prior history of diarrhea before administration of the antibiotic. In fact, the more severe cases of

colitis had a history of chronic constipation prior to antibiotic therapy. Tedesco and co-workers (1974, p. 429), believe that an adequate bowel history could not be delineated from the previous studies reported in the literature, and therefore interviewed all patients at their institution who received clindamycin in a six month period. The interview gave special attention to the prior bowel habits of the patients. They found that none of the patients who developed antibiotic-induced pseudomembranous colitis had a prior history of diarrhea. In the study by Davis (1974, p. 16), only one patient had a history of occasional loose stools before the development of antibiotic-induced pseudomembranous colitis and this was reported to be secondary to diverticular disease.

Seventeen of the nineteen patients in the study hospital were reported to have "normal" elimination habits prior to the onset of symptoms. In one patient it was noted that there was history of "irritable bowel syndrome", while one patient had "chronic constipation". Thus, most patients in the literature and in the study hospital did not have a history of bowel disease prior to the administration of antibiotics.

Reasons for Antibiotic Therapy

From the literature, it was found that the broad-spectrum antibiotics were incriminated as causative agents in pseudomembranous colitis. These drugs were administered for a variety of illnesses (table 7).

TABLE 7

REASONS FOR RECEIVING ANTIBIOTICS OF CASES WITH
ANTIBIOTIC-INDUCED PSEUDOMEMBRANOUS COLITIS
FROM REVIEWED LITERATURE

Number of Patients (Percent of Number of Patients)

STUDY	YEAR	NUMBER OF CASE STUDIES	RESPIRATORY INFECTIONS	* OTHER INFECTIONS	DENTAL	SURGERY
Koltz et. al.	1953	5	1	1	--	1
Cohen et. al.	1973	3	1	1	--	1
Schapiro and Newman	1973	4	3	1	--	--
Davis	1974	4	2	1	1	--
Hakkal	1974	2	1	1	--	--
Viteri et. al.	1974	7	6	--	--	1
Berkowitz et. al.	1975	1	1	--	--	--
Butsch et. al.	1975	1	--	--	--	1
Summer and Tedesco	1975	23	5	9	2	7

TABLE 7

Reasons for Receiving Antibiotics of Cases with
Antibiotic-Induced Pseudomembranous Colitis
From Reviewed Literature (continued)

Number of Patients (Percent of Number of Patients)

STUDY	YEAR	NUMBER OF CASE STUDIES	RESPIRATORY INFECTIONS	* OTHER INFECTIONS	DENTAL	SURGERY
Theodoropoulos et. al.	1975	1	1	--	--	--
Goodacre et. al.	1977	2	2	--	--	--
TOTALS		53	23(43)	14(26)	3(6)	11(21)

*Includes such infections as sinusitis, suspected amebiasis, and cellulitis.

However, almost 50 percent of the patients who developed antibiotic-induced pseudomembranous colitis received the offending drug for some form of respiratory infection such as pneumonia, viral illness, or "bronchitis". Various other types of infections accounted for the next most frequent category. Twenty-six percent of the patients received the offending antibiotic for such infections as sinusitis, suspected amebiasis, cellulitis, diabetic ulceration of the extremity, or dermatitis. Twenty-one percent of the patients from the reviewed literature developed antibiotic-induced pseudomembranous colitis in association with therapy at the time of a surgical procedure. In some, antibiotic was administered prophylactically while other patients received the antibiotic for post-surgical infections.

Respiratory infections, which were often nonbacterial, again accounted for over 50 percent of the infections for which the offending antibiotic was administered in the study hospital (table 8). Other infections again were the second leading cause of antibiotic administration. In the study hospital, the antibiotic that caused the most pseudomembranous colitis was administered for such reasons as "flu", upper respiratory infections, pneumonia, sore throat and cold-like symptoms, and post-surgical wound infection. Only two patients developed the disease in association with antibiotic therapy at the time of surgery and none developed the disease in association with dental therapy.

TABLE 8

REASONS FOR RECEIVING ANTIBIOTICS IN CASES WITH
ANTIBIOTIC-INDUCED PSEUDOMEMBRANOUS COLITIS
IN STUDY HOSPITAL JANUARY 1970 - JUNE 1977

Number of Patients (Percent of Number of Patients)

CASE NO.	RESPIRATORY INFECTION	OTHER* INFECTIONS	SURGERY
1	+	--	--
2	+	--	--
3	--	+	--
4	--	+	--
5	--	+	--
6	+	--	--
7	+	--	--
8	--	+	--
9	+	--	--
10	+	--	--
11	+	--	--
12	--	--	+
13	+	--	--
14	+	--	--
15	+	--	--

TABLE 8
 Reasons for Receiving Antibiotics in Cases with
 Antibiotic-Induced Pseudomembranous Colitis
 In Study Hospital January 1970 - June 1977 (continued)

CASE NO.	RESPIRATORY INFECTION	OTHER INFECTIONS	SURGERY
16	+	--	--
17	--	+	--
18	--	--	+
19	+	--	--
	12(63)	5(26)	2(10)

Although, various reasons were noted for the use of the antibiotics, the two most common reasons as noted on tables 7 and 8 were respiratory infections and other infections. Respiratory infections comprised 43 percent of the population, while other infections were noted in over a quarter of the reviewed cases. From the study hospital similar findings of the various infections was noted with just over one-fourth of the records noted this to be the reasons for the antibiotic therapy. However, there was a greater number of respiratory infections noted in the study hospital than in literature with over 60 percent of the patients identifying respiratory problems as the initial illness for which the antibiotic was administered.

Physical Examination

The physical examinations of patients with antibiotic-induced pseudomembranous colitis was noted in the literature to be abnormal in three basic respects: fever, abnormal abdominal examination (tenderness, distention, and/or altered bowel sounds), and abnormal proctoscopic examination (table 9). The topic of fever has previously been analyzed under the sub-heading "Chief Complaint and Clinical Manifestations."

In 46 percent of the patients from the reviewed literature, positive abdominal findings were noted (table 9). These ranged from

TABLE 9

INITIAL PHYSICAL EXAMINATION FINDINGS OF CASES
WITH ANTIBIOTIC INDUCED PSEUDOMEMBRANOUS
COLITIS IN REVIEWED LITERATURE

Number of Patients (Percent of Number of Patients)

STUDY	YEAR	NUMBER OF CASE STUDIES	POSITIVE * ABDOMINAL EXAMINATION	POSITIVE ** PROCTOSCOPIC FINDINGS
Manashil and Kern	1973	3	3	3
Pittman et. al.	1973	16	0	16
Schapiro and Newman	1973	4	1	4
Davis	1974	4	NR ***	4
Hakkal	1974	2	2	2
Viteri et. al.	1974	7	6	7
Berkowitz et. al.	1975	1	0	1
Butsch et. al.	1975	1	1	1
Tedesco et. al.	1975	8	8	8
TOTALS		46	25(54)	46(100)

* Includes abdominal distention, tenderness, and abnormal bowel sounds.

** Includes edema, friability, ulceration, exudate, and pseudomembranes.

*** NR = Not recorded.

vague non-specific tenderness to severe abdominal tenderness.

Although no instance of rigidity was reported, some rebound discomfort was noted with palpation at the time of the physical examination (Tedesco et. al. 1975, p. 481).

The most important and confirmatory finding in the physical examination were those of the proctoscopic examinations. All patients in the reported literature had an abnormal proctoscopic examination (table 9). On digital examination, it was also noted that some patients had moderate to severe perianal irritation (Pittman et. al. 1974, p. 368). As noted by Summer and Tedesco (1975, p.237), the positive proctoscopic findings were characterized by discrete elevated plaque-like lesions. These yellow-whitish areas were adherent to a red, edematous and often friable mucosa. These punctate areas were estimated to measure from two to five millimeters in size, although some pseudo-membranes may measure up to two centimeters in diameter (Berkowitz et. al. 1975, p. 362).

In the present study, similar findings were extracted from the review of the medical records in the study hospital. However, only one case of the nineteen reviewed (a young woman who was six months pregnant) had any type of surgical intervention or even a surgical consultation. One case took some two weeks before the prior use of

lincomycin was discovered. The remainder of the cases were evident from the beginning since the majority were referrals.

Unlike the cases in the reviewed literature in which only 44 percent had positive abdominal findings (table 9), in the study institution, 79 percent of the patients had some type of abdominal finding at the time of the physical examination (table 10).

These findings concurred with those noted in the literature, i.e., lower abdominal pain, hypogastric pain, and elevations of temperature (Cohen et. al. 1973, p. 137; Tedesco et. al. 1975, p. 481). All proctoscopic examinations at the study institution were consistent with the diagnosis of pseudomembranous colitis. Thirty-seven percent of the patients had findings compatible with a resolving disease, but with a past history of antibiotic usage prior to the diarrhea, a final diagnosis of antibiotic-induced pseudomembranous colitis was made.

Initial Diagnosis

No study in the literature tabulated the initial clinical diagnosis of patients with antibiotic-induced pseudomembranous colitis. In the study institution, the initial impression or diagnosis was post-antibiotic or antibiotic-induced diarrhea, in 74 percent of the cases. In one case, antibiotic usage was not initially identified because the patient and the family had not been informed that the drug had been administered and the records of previous treatment elsewhere were unavailable. In

TABLE 10

INITIAL PHYSICAL EXAMINATION FINDINGS OF CASES WITH
ANTIBIOTIC-INDUCED PSEUDOMEMBRANOUS COLITIS
IN STUDY HOSPITAL JANUARY 1970 - JUNE 1977

Number of Patients (Percent of Number of Patients)

CASE NO.	*ABDOMINAL EXAMINATION	**PROCTOSCOPIC EXAMINATION
1	+	+
2	+	+
3	+	+
4	+	+
5	-	+
6	-	+
7	+	+
8	+	+
9	-	+
10	+	+
11	+	+
12	+	+
13	+	+
14	+	+
15	+	+
16	+	+

TABLE 10
Initial Physical Examination Findings of Cases With
Antibiotic-Induced Pseudomembranous Colitis
In Study Hospital January 1970 - June 1977 (continued)

CASE NO.	*ABDOMINAL EXAMINATION	**PROCTOSCOPIC EXAMINATION
17	+	+
18	+	+
19	-	+
	15(79)	19(100)

* Includes abdominal distention, tenderness and abnormal bowel sounds.

** Includes edema, friability, ulceration, exudate and pseudomembranes.

one case the complaint of diarrhea was considered to be a minor problem and the disease was discovered at the time of proctoscopy. Thus in almost three-fourths of the patients in the study hospital, the initial diagnosis was derived from an adequate history and physical examination, thereby preventing further complications and possibly an unnecessary operation. It has been previously noted that early diagnosis and subsequent prompt treatment is warranted in an attempt to prevent the possible complication of antibiotic-induced pseudomembranous colitis.

Laboratory Data

There have been no consistently reported positive hematologic findings that may be beneficial in the diagnosis of antibiotic-induced pseudomembranous colitis, although in one study it was reported that significant changes in the serum glutamic oxaloacetic transaminase (SGOT) and the alkaline phosphatase were noted (Butsch et. al. 1974, p. 153). However, no other studies from the literature appeared to confirm this finding. Leukocytosis was noted by several authors and varied from 9000 to 37,500 white blood cells per cubic millimeter (Schapiro and Newman 1973, p. 163; Viteri et. al. 1974, p. 1137; Tedesco et. al. 1975, p. 481; Berkowitz et. al. 1975, p. 362). There were no significant changes noted in the differential white blood cells count in the patients reported in the literature.

In the study hospital, 53 percent of the reported cases had a leukocytosis, but only one case had a slight shift to the left in the differential count. The alkaline phosphatase was elevated in 47 percent of the reviewed cases. In only 37 percent was the SGOT noted to be elevated in the present study (table 11).

It was noted in the literature that the electrolyte group may become abnormal in antibiotic-induced pseudomembranous colitis (Tedesco et. al. 1974, p. 429; Viteri et. al. 1974, p. 1137; Tedesco et. al 1975, p. 481). However, in the present study there were no electrolyte disturbances noted. In most of the cases in the literature, stool for culture was obtained and was negative in all cases. In the study hospital, stools for culture and/or for ova and parasite were obtained in 79 percent of the cases and in no instance were they positive.

The barium enema and a plain film of the abdomen were the only two significant positive diagnostic radiologic procedures noted in the reviewed literature (table 12). An abnormal barium enema was noted in 78 percent of the reported cases from the literature. The most common findings were that shaggy, edematous mucosa with ulcerations and excessive amounts of mucous secretion (Theodoropoulos et. al. 1975, p. 435; Hakkal 1975, p. 78). Pseudopolyp formation was present in an occasional case (Schapiro and Newman 1973, p. 263; Viteri et. al. 1974, p. 1137). Although positive radiologic findings may be noted to occur in

TABLE 11

HEMATOLOGIC FINDINGS OF CASES WITH ANTIBIOTIC-INDUCED
PSEUDOMEMBRANOUS COLITIS IN STUDY HOSPITAL
JANUARY 1970 - JUNE 1977

Number of Patients (Percent of Number of Patients)

CASE NO.	WHITE BLOOD COUNT	ALKALINE PHOSPHATASE	SERUM GLUTAMIC OXALOACETIC TRANSAMINASE
1	+	-	-
2	+	+	+
3	-	-	-
4	-	+	+
5	-	-	-
6	-	+	+
7	+	+	-
8	+	-	-
9	-	+	-
10	+	+	+
11	-	+	+
12	-	-	-
13	+	+	-
14	+	-	-
15	+	-	+

TABLE 11
Hematologic Findings of Cases With Antibiotic-Induced
Pseudomembranous Colitis in Study Hospital
January 1970 - June 1977 (continued)

CASE NO.	WHITE BLOOD COUNT	ALKALINE PHOSPHATASE	SERUM GLUTAMIC OXALOACETIC TRANSAMINASE
16	+	+	-
17	+	-	-
18	-	-	+
19	-	-	-
	10(53)	9(47)	7(37)

+ = elevated

- = normal

TABLE 12

RADIOLOGIC FINDINGS OF CASES WITH ANTIBIOTIC-INDUCED
PSEUDOMEMBRANOUS COLITIS IN REVIEWED LITERATURE

Number of Patients (Percent of Number of Patients)

STUDY	YEAR	NUMBER OF CASE STUDIES	ABNORMAL BARIUM ENEMA	ABNORMAL FLAT PLATE OF ABDOMEN
Cohen et. al.	1973	3	1	NR
Manahil and Kern	1973	3	3	NR
Shapiro and Newman	1973	4	4	NR
Davis	1974	4	3	0
Hakkal	1974	2	2	0
Viteri et. al.	1975	7	4	4
Berkowitz et. al.	1975	1	1	1
Butsch et. al.	1975	1	1	1
Theodoropoulos et. al.	1975	1	NR	0
Goodacre et. al.	1977	2	2	2
TOTALS		29	21(78)	8(28)

NR = Not Recorded

antibiotic-induced pseudomembranous colitis, they can not be differentiated from other acute inflammatory processes of the colon. The plain film of the abdomen was noted to be abnormal in just over a quarter of the reported cases (table 13)

The barium enema examination in the study institution did not correspond with the computed findings from the literature in the percentage of abnormal findings (table 13). In the study hospital, only 32 percent of the total patients had an abnormal colon examination. In one case pseudopolyp formation was noted to have occurred. The plain film of the abdomen was, however, similar in its frequency of positivity, i.e., approximately a quarter of the study patients had an abnormal plain film of the abdomen (table 13).

Although the literature notes that there is an elevation in the leukocyte count, none of the studies gave a specific percentage of patients that developed leukocytosis. In the study hospital, it was noticed that over 50 percent of the patients reviewed had an abnormal white blood count. As with the leukocytosis, the literature alluded to elevations in the alkaline phosphatase and the serum glutamic oxaloacetic transaminase, however, there was no mention of the percentage of patients that had elevations. It was found in the study hospital that 47 percent and 37 percent respectively had elevated values. Radiologically the literature differed with the findings of the study hospital on the abnormal colon examinations. In the literature, over three-fourths of

TABLE 13

RADIOLOGIC FINDINGS OF CASES WITH ANTIBIOTIC-INDUCED
PSEUDOMEMBRANOUS COLITIS IN STUDY HOSPITAL
JANUARY 1970 - JUNE 1977

Number of Patients (Percent of Number of Patients)

CASE NO.	BARIUM ENEMA	FLAT PLATE OF ABDOMEN
1	+	-
2	+	+
3	+	ND
4	-	ND
5	ND	ND
6	-	-
7	+	+
8	-	-
9	-	-
10	+	+
11	-	ND
12	-	-
13	-	ND
14	+	+
15	-	ND
16	ND	ND

TABLE 13
 Radiologic Findings of Cases With Antibiotic-Induced
 Pseudomembranous Colitis in Study Hospital
 January 1970 - June 1977 (continued)

CASE NO.	BARIUM ENEMA	FLAT PLATE OF ABDOMEN
17	-	ND
18	-	-
19	-	ND
TOTALS	6(32)	5(26)

+ = Positive finding
 - = Negative finding
 ND = Not Done

the cases had abnormal findings on the colon examination. However, this was not noted in the study institution, in which only 32 percent of the patients had abnormal findings. Similar findings though were noted in the findings of the flat plate or plain film of the abdomen. Both were noted to have just over 25 percent of the patients with abnormal findings.

Therapy

The reviewed literature cited many therapeutic modalities for antibiotic-induced pseudomembranous colitis (table 14). These ranged from the use of other antibiotics, which accounted for 7 percent of the total patient population, to the use of antidiarrheal agents which comprised 56 percent of the total (table 14). When it was believed that staphylococcal overgrowth was the causative factor of the diarrhea, Vancomycin or Kanamycin was administered. Other antibiotics which were utilized were Keflin, and Mycostatin. Of the antidiarrheal agents, Lomotil was the most commonly used, although there were cases in which Kaopectate was utilized (Pittman et. al. 1974, p. 368). Considerable controversy still exists with respect to the value of this mode of therapy. Lomotil has been shown to increase the possibility of blood in the stool (Theodoropoulos et. al. 1975, p. 435) and to possibly increase the severity of the diarrhea after this therapy is discontinued (Pittman et. al. 1974, p. 367).

TABLE 14

TREATMENT MODALITIES OF CASES WITH ANTIBIOTIC-INDUCED
PSEUDOMEMBRANOUS COLITIS IN REVIEWED LITERATURE***

Number of Patients (Percent of Number of Patients)

STUDY	YEAR	NUMBER OF CASE STUDIES	ANTI- DIARRHEAL AGENTS	STEROIDS*	CONSERVATIVE THERAPY**	ANTI- BIOTIC
Cohen et. al.	1973	3	-	1	1	1
Pittman et. al.	1973	16	2	4	-	-
Manashil and Kern	1973	3	2	-	1	-
Schapiro and Newman	1973	4	-	2	4	-
Davis	1974	4	-	2	1	1
Hakkal	1974	2	-	-	2	-
Viteri et. al.	1974	7	5	1	3	3
Berkowitz et. al.	1975	1	-	-	1	-
Butsch et. al.	1975	1	-	-	1	-

TABLE 14
Treatment Modalities of Cases With Antibiotic-Induced
Pseudomembranous Colitis in Reviewed Literature*** (continued)

Number of Patients (Percent of Number of Patients)

STUDY	YEAR	NUMBER OF CASE STUDIES	ANTI- DIARRHEAL AGENTS*	STEROIDS	CONSERVATIVE THERAPY**	ANTI- BIOTIC
Summer and Tedesco	1975	23	23	-	23	-
Tedesco et. al.	1975	8	7	-	7	-
Theodoropoulos et. al.	1975	1	1	-	-	-
Goodacre et. al.	1977	2	2	-	-	-
TOTAL		75	42(56)	10(14)	44(59)	5(7)

* Given orally, intravenously or per rectum

** Includes intravenous fluids and electrolyte replacement

*** Consists of patients who were treated with multiple forms concomitantly

Steroids were also used in the treatment of this disease in 58 percent of the cases in the literature. These steroids were administered in various forms, e.g., Hydrocortisone intravenously, Prednisone orally, and Annusol suppository per rectum. Occasionally, an injection of ACTH was noted to have some therapeutic value (Schapiro and Newman 1973, p. 263; Hakkal 1974, p. 78). However, in these cases there were no significant improvement in the patient's condition after receiving the ACTH injections.

In the study hospital, conservative treatment was the most common single form of therapy. Conservative treatment consisted of intravenous fluids, food restriction, and electrolyte monitoring with replacement as needed. In one case, no treatment was initiated as the illness was resolving at the time the patient was seen in the study hospital. Approximately one-third of the patients were treated conservatively (table 15). Steroids or an antidiarrheal agent were the next most commonly used therapeutic modality. These each comprised just over one-quarter of the cases at the study hospital. As in the literature, various steroid preparations were administered either orally, intravenously, or rectally. There was no significant difference in the duration of the disease between those patients treated with steroids or antidiarrheal agents and those treated by conservative therapy in the study hospital.

TABLE 15

TREATMENT MODALITIES OF CASES WITH ANTIBIOTIC-INDUCED
PSEUDOMEMBRANOUS COLITIS IN STUDY HOSPITAL
JANUARY 1970 - JUNE 1977

Number of Patients (Percent of Number of Patients)

CASE NO.	ANTI-DIARRHEAL AGENTS	STEROIDS	CONSERVATIVE THERAPY*	ANTI-BIOTICS
1	-	+	-	-
2	-	+	-	+
3	-	+	-	-
4	+	-	-	-
5	+	-	-	-
6	-	-	+	-
7	-	-	+	-
8	+	-	-	-
9	-	-	+	-
10	-	+	-	+
11	-	-	-	+
12	-	-	-	+
13	+	-	-	-
14	+	-	-	-
15	-	+	-	-

TABLE 15
 Treatment Modalities of Cases With Antibiotic-Induced
 Pseudomembranous Colitis in Study Hospital
 January 1970 - June 1977 (continued)

Number of Patients (Percent of Number of Patients)

CASE NO.	ANTI- DIARRHEAL AGENTS	STEROIDS	CONSERVATIVE THERAPY*	ANTI- BIOTICS
16	-	-	+	-
17	-	-	+	-
18	-	-	+	-
19**	-	-	-	-
TOTAL	5(26)	5(26)	6(32)	4(21)

* Includes intravenous fluids, food restriction, and electrolyte replacement.

** Asymptomatic patient at the time of evaluation.

In the literature, both antidiarrheal agents and conservative treatment were used in similar percentage ratings in the treatment of the patients. Both of these treatment modalities were used in over 50 percent of the cases reviewed. However, in the study hospital, none of the different modalities were used in over 50 percent of the patients. Although the most used treatment in the study hospital was noted to be the conservative treatment with 32 percent of the patients receiving this form of therapy. Therefore, as noted by the reviewed literature, no specific form of therapy has been accepted by the various studies.

Follow-up Care and Outcome

Follow-up care of patients with antibiotic-induced pseudomembranous colitis in the reviewed literature consisted of repeated assessments including serial proctoscopic examinations to complete resolution of the clinical features. All the patients were followed from two to six months after remission (Tedesco et. al. 1974, p. 429; Viteri et. al. 1974, p. 1137). In the study hospital, similar follow-up care was noted with serial proctoscopic exams performed till normal. The reviewed literature reported only four cases in which antibiotic-induced pseudomembranous colitis could be related to the death of the patient (Scott et. al. 1974, p. 1232; Summer and Tedesco 1975, p. 237). In the study hospital, no related deaths were noted. In one case, the patient died from a previous diagnosed cancer of the bladder.

Summary

Variables extracted from the reviewed literature were compared, by relative frequency, to those found in the study institution. Various clinical, historical, and laboratory findings were compared. Although slight differences were noted in some of the percentages, there were no striking differences between the literature and the study institution.

Nineteen records of patients diagnosed with antibiotic-induced pseudomembranous colitis were reviewed. The review revealed that twice as many women were afflicted with this disease entity than were men. It was also noticed that the elderly, between sixty and sixty-nine were affected more often than all the other age groups combined in this study. All the patients reviewed were of the caucasian race.

The antibiotics that were incriminated the most in the study hospital were lincomycin and clindamycin. The two broad-spectrum antibiotics were noted to have been used prior to the onset of diarrhea in more cases than the other antibiotics combined. The average length of therapy of these two drugs was one week. With number of days from initiation of therapy to onset of symptoms ranging from one day to nearly three weeks.

The chief complaint of diarrhea associated with abdominal pain was evident in the study population. This was the same as the ones from the previous studies reviewed. Previous bowel history from the study hospital and the literature was non-contributory in determining the possible etiology of this disease.

Respiratory infections coupled with various infections were the major reasons given for receiving the antibiotic therapy in both the reviewed literature and the study institution. On physical examination, the basic examination was considered to be normal in the literature and in the study hospital. However, it was noted that the only positive findings were those of vague abdominal tenderness and an abnormal proctoscopic examination. The abdominal tenderness could not be localized on most of the patients nor was there any radiation elicited from the patients. The abnormal findings of the proctoscopic procedure were those consistent with the diagnosis of pseudomembranous colitis, although the initial diagnosis was that of antibiotic-induced diarrhea in the study hospital.

Laboratory data that were noted to be abnormal at the study institution were the white blood count in which elevation ranged from mild increases to marked elevations. Other abnormal findings were noted in the alkaline phosphatase and in the serum glutamic oxaloacetic transaminase (SGOT). Although the barium enema was reported in the

literature to be abnormal in a majority of the cases, this finding could not be substantiated in the study hospital. The plain film of the abdomen was also noted to be abnormal in this disease. But this finding was noted in less than 30 percent of the patients making a poor diagnostic procedure in this disease.

Therapy in these patients was just as varied in the study hospital as was noted in the literature. This ranged from no treatment in the asymptomatic patient to the use of steroids and intravenous fluids in the study hospital. Thus not providing any solution to the problem of how to handle patients through medical treatment.

Follow-up was provided to the patients at the study hospital in the form of serial proctoscopic and/or colon examinations with barium. The average duration of this disease in the study hospital was slightly less than as reported in the literature. The course averaged four weeks in the study hospital as compared to six weeks in the literature.

Although a few deaths were reported to have been the results of the illness in the literature, no directly related deaths were noted in the present study.

CHAPTER V

SUMMARY, CONCLUSIONS, IMPLICATIONS, AND RECOMMENDATIONS

Summary

An analytical review of the medical records of persons with a diagnosis of antibiotic-induced pseudomembranous colitis was conducted in three separate parts.

First, the pertinent literature regarding antibiotic-induced pseudomembranous colitis was reviewed. From this review, specific variables were extracted and compiled into overall percentage ratings of incidence. The variables from the reviewed literature were then broadened to include additional variables that had not previously been reported in cases of antibiotic-induced pseudomembranous colitis.

Next, data from the medical records of patients with a diagnosis of antibiotic induced pseudomembranous colitis were collected from a large referral center in Central Texas. The records utilized were those from January 1970, when the disease entity was first clearly documented at the study institution, to June 1977, when the present study was

completed. The data were obtained from the review of nineteen patients' records with documented antibiotic-induced pseudomembranous colitis and were tabulated by the incidence of frequency.

Then, the findings from the study hospital were compared with the findings from the reviewed literature. From the comparison, an assessment tool was developed for use by the clinical nurse specialist in the long-term follow-up care of patients with antibiotic-induced pseudomembranous colitis.

Conclusions

From the set of criteria extracted from a review of the literature and subsequent comparison with the study hospital, the following conclusions for this study were drawn:

1. From the literature, the average incidence of antibiotic-induced colitis of patients administered antibiotics in one study proved to be 10 percent. However, due to the retrospective nature of the present study, this finding could not be compared.

2. The literature findings showed a modest female predominance in antibiotic-induced pseudomembranous colitis. In the study hospital, twice as many women were noted to develop this illness as men. Some articles in the reviewed literature noted two distinct age groups in antibiotic-induced pseudomembranous colitis--a younger group

and an elderly group. The findings from the study institution revealed a single predominant age grouping in the seventh decade of life.

3. In the literature reviewed, several antibiotic agents were noted to play a causative role in this disease. Lincomycin and its derivative compound clindamycin were the most commonly incriminated antibiotics. The findings from the study hospital revealed that lincomycin and clindamycin were the causal antibiotic in antibiotic-induced pseudomembranous colitis more often than the other antibiotics combined.

4. Diarrhea was noted to be the initial complaint of all the patients in the reviewed literature. Abdominal pain was noted in 93 percent of the total. Similar findings were noted in the study institution.

5. The patients in the literature in which a bowel history was elicited had no prior history of diarrhea. The similar findings were identified in this study.

6. Of the several reasons given in the literature for the administration of various antibiotics, respiratory infections comprised 43 percent of the total. In the study hospital this indication for antibiotic administration was also noted to be the predominant reason for antibiotic administration.

7. The positive findings in the physical examination from the literature were the abdominal and proctoscopic examinations. In the study hospital, the abdominal examination was noted to be more frequently positive than in the cases cited in the literature. However, all patients in the reviewed literature and the study hospital had a positive and diagnostic proctoscopic examination.

8. Although no studies in the reviewed literature noted the initial diagnosis in the study hospital the diagnosis of antibiotic-induced diarrhea was reported in nearly three-quarters of the patients.

9. The literature revealed only one consistent hematologic finding that was seen in antibiotic-induced pseudomembranous colitis. This was an elevated white blood count which was also noted in the study hospital. The literature noted occasional elevations in the alkaline phosphatase and in the serum glutamic oxaloacetic transaminase (SGOT). Similar findings were noted in the study institution with nearly 50 percent having elevations in the alkaline phosphatase and over a third with elevations in their SGOT levels.

10. In the reviewed literature, over three-quarters of the patient population had an abnormal barium enema. However, in the study hospital, only thirty-two percent of the patients had a positive colon examination.

11. From the literature no definitive treatment modality could be elucidated. In as much as antidiarrheal agents and conservative therapy were used as often as the next one. Also, there remains some doubt in the therapeutic values. Similar findings were noted in the study hospital and the appropriate therapeutic modality for antibiotic-induced pseudomembranous colitis, if any, remains in doubt.

12. The literature noted cases of mortality in which antibiotic-induced pseudomembranous colitis played a significant role. The study hospital did not have any deaths directly related to antibiotic-induced pseudomembranous colitis.

Implications

The ultimate objective of this study was to provide the clinical nurse specialist with a specific assessment tool to be used in the long-term care of patients with antibiotic-induced pseudomembranous colitis. This tool could be utilized by the clinical nurse specialist, functioning in such clinical settings as an outpatient clinic, a gastroenterology department, hospital care, convalescent care settings, or a public health clinic.

Due to the possibility of morbidity, and even rarely mortality, associated with antibiotic therapy, health care professionals at all levels of health care delivery must be constantly vigilant for these

adverse reactions. Through this attitude, appropriate and prompt therapy may be initiated in order to prevent or lessen subsequent complications. Post-acute evaluations may be required to document any alteration of the patient's subsequent condition. Therefore, an adequate and regular interim history and physical examination should be accomplished in these patients until their condition is completely resolved, and this resolution is documented.

A complete history and thorough physical examination should always be performed on an ill patient. The history must be compulsively elicited, no matter the presenting complaint, and must include drug usage. The review of systems must be complete if one is to elicit the ultimate nature of a patient's disease.

Of the many roles identified for clinical nurse specialist in previous chapters, the roles of practitioner, consultant, and teacher are the most important. All too often, it is the nurse who first identifies a specific patient problem or complaint. In the example of antibiotic-induced pseudomembranous colitis, the complaint may be diarrhea or abdominal pain. It is important that not only the clinical nurse specialist understand the disease process and its implications, but also that any nurse be able to identify the early symptoms of this disease. Early diagnosis and prompt action on the part of the nurse could prevent many of the devastating complications seen in antibiotic-induced

pseudomembranous colitis. Thus an adequate knowledge of the signs, symptoms, and complications of this disease is warranted. Total care of the patient no longer means bedside care on an eight-hour basis. The nurse today must be willing to accept the responsibilities of long-term care of any patients on a twenty-four hour basis.

Recommendations

Recommendations for further study are:

1. Further evaluation and broadening of studies to obtain a true racial incidence for antibiotic-induced pseudomembranous colitis should be implemented.
2. There should be a study conducted on the overall incidence of antibiotic-induced pseudomembranous colitis in hospital admissions.
3. There should be utilization and evaluation of the proposed assessment tool.
4. There should be a double-blind study to compare the relative merits of various anti-inflammatory agents and to determine their value, if any, in the treatment of antibiotic-induced pseudomembranous colitis.
5. A double-blind study to compare the merits, if any, of various forms of antidiarrheal therapy should be considered.

6. There should also be further study in order to answer the following questions:

a. What is the mechanism or mechanisms which produce this disease entity?

b. Does previous bowel surgery have a predisposing relationship to the development of antibiotic-induced pseudomembranous colitis?

c. Is there a hereditary predisposition to the development of antibiotic-induced pseudomembranous colitis?

APPENDIX A

TEXAS WOMAN'S UNIVERSITY
COLLEGE OF NURSING
DENTON, TEXAS

DALLAS CENTER
1810 Inwood Road
Dallas, Texas 75235

HOUSTON CENTER
1130 M.D. Anderson Blvd.
Houston, Texas 77025

AGENCY PERMISSION FOR CONDUCTING STUDY*

THE Scott and White Hospital and Clinic

GRANTS TO Daniel J. Werlinger

a student enrolled in a program of nursing leading to a Master's Degree at Texas Woman's University, the privilege of its facilities in order to study the following problem:

A Nursing Assessment Tool For Follow-up Care of Antibiotic-Induced Pseudomembranous Colitis.

The conditions mutually agreed upon are as follows:

1. The agency (may) (~~may not~~) be identified in the final report.
2. The names of consultative or administrative personnel in the agency (may) (~~may not~~) be identified in the final report.
3. The agency (wants) (~~does not want~~) a conference with the student when the report is completed.
4. The agency is (willing) (~~unwilling~~) to allow the completed report to be circulated through interlibrary loan.
5. Other: _____

Date

June 2/77

Dan Werlinger
Signature of student

Lillian E. Achilles
Signature of Agency Personnel

Mona M. Counts
Signature of Faculty Advisor

*Fill out and sign three copies to be distributed as follows: Original -- Student; first copy -- agency; second copy -- T.W.U. College of Nursing.

APPENDIX B

CRITERION

1. What is the incidence of antibiotic-induced pseudomembranous colitis as the disease relates to sex, age and race?
2. What are the most common causative antibiotic agents in pseudomembranous colitis?
3. What are the early manifestations of antibiotic-induced pseudomembranous colitis?
4. Does a previous bowel disorder predispose one to antibiotic-induced pseudomembranous colitis?
5. What are the positive findings noted on physical examination of patients with antibiotic-induced pseudomembranous colitis.
6. What laboratory tests, if any, are abnormal in antibiotic-induced pseudomembranous colitis and are they of value in the diagnosis of this disease?
7. What roentgenologic studies, if any, are significant in the diagnosis of antibiotic-induced pseudomembranous colitis?
8. What is the magnitude of the diarrhea in antibiotic-induced pseudomembranous colitis?

9. What are the most beneficial treatment modalities in antibiotic-induced pseudomembranous colitis?
10. What is the duration of symptoms in antibiotic-induced pseudomembranous colitis?

APPENDIX C

ASSESSMENT TOOL FOR USE BY CLINICAL NURSE SPECIALIST IN LONG-TERM CARE OF PATIENTS WITH A DIAGNOSIS OF ANTIBIOTIC-INDUCED PSEUDOMEMBRANOUS COLITIS

NOTE: It is assumed that a complete history and physical examination will have been performed at the time of the original diagnosis of antibiotic-induced pseudomembranous colitis. However, in the event that no history and physical examination was performed or that it is inadequate, a complete history and physical examination will be done at the time of the first client contact.

Subsequently, an interim history and physical examination with special attention to those specific areas involved in the disease entity will be conducted. These include the following:

A. Interview History

1. Stools

- a. Number/Day _____
- b. Blood or Melena? Yes _____ No _____
(If yes, indicate quantity) _____

2. Abdominal Pain: Yes _____ No _____
(If yes, indicate below)

- a. Character _____
- b. Duration _____
- c. Location _____
- d. Radiation _____
- e. Aggravating Factors _____
- f. Relieving Factors _____

B. Drugs presently taken (List name, quantity, and duration)

C. Improvement? (Check one)

- 1. Stable _____
- 2. Improved _____
- 3. Worse _____

D. Physical Examination of abdomen (Dash if absent, explain if present)

1. Abdominal tenderness

- a. Location _____
- b. Radiation _____

2. Rigidity _____

3. Rebound _____

4. Masses or organomegaly _____

5. Bowel sounds: Normal _____ Abnormal _____

Absent _____

Hypoactive _____

Hyperactive _____

"tinkling" _____

"rushing" _____

E. Rectal and proctoscopic examination: (Check appropriate answer)

1. Perianal examination

- a. Perianal irritation: Yes _____ No _____
 b. External hemorrhoids: Yes _____ No _____

2. Digital examination

- a. Pain on insertion: Yes _____ No _____
 b. Internal hemorrhoids: Yes _____ No _____
 (1) Masses: Yes _____ No _____

(If yes, indicate approximate size and shape)

(2) Stool examination

- (a) Color _____
 (b) Consistency _____
 (c) Test for occult blood:
 Positive _____
 Negative _____

3. Proctoscopic examination:

Appearance of Mucosa: Normal _____
 Abnormal _____
 (If abnormal, describe findings below)

- a. Edematous: Yes _____ No _____
 b. Erythema: Yes _____ No _____
 c. Ulceration: Yes _____ No _____
 (If yes, describe size and location)

- d. Exudate: Yes _____ No _____
 (If yes, describe character and color)

- e. Friability: Yes _____ No _____
 (If yes, describe how easy it is to elicit)

- f. Pseudomembranes: Yes _____ No _____
 (If yes, describe size and Location)

BIBLIOGRAPHY

- Altemeier, William A., Hummel, Robert P., and Hill, Edward O. 1963. Staphylococcal Enterocolitis Following Antibiotic Therapy. Annals of Surgery. 157:847-857.
- American Nurses' Association. Congress for Nursing Practice. 1974.
- Aradine, Carolyn R. and Denyes, Mary J. 1972 Activities and Pressures of Clinical Nurse Specialists. Nursing Research. 21:411-418.
- Azar, Hormoz and Drapanas, Theodore. 1968. Relationship of Antibiotics to Wound Infection and Enterocolitis in Colon Surgery. American Journal of Surgery. 115:209-215.
- Bartlett, John G. and Gorbach, Sherwood L. 1975. Treatment of Aspiration Pneumonia and Primary Lung Abscess. Journal of The American Medical Association. 234:935-937.
- Bartlett, John G. 1976. Anaerobic Infections. Hospital Medicine.
- Berkowitz, Daniel, Bezahler, G. and Brandt, Lawrence. 1975. Ampicillin-associated Colitis. The American Journal of Gastroenterology. 362-365.
- Berlinger, Marine R. 1973. The Preparation and Roles of the Clinical Specialist at the Master's Level. Cited in Riehl and McVay, The Clinical Nurse Specialist, New York, Meredith Co.
- Birnbaum, D., Laufer, A. and Freund, M. 1961. Pseudomembranous Enterocolitis. A Clinicopathologic Study. Gastroenterology. 41: 345-351.
- Briggs, Rambie L. Scott and White Memorial Hospital, Temple, Texas. Interview. May 17, 1977.
- Butsch, John L., Al-Humadi, Adil H., Alford, Edwin. 1975. Clindamycin Colitis Following Clindamycin Therapy: Report of a Case. Disease of the Colon and Rectum. 18:152-157.

- Cohen, Leroy E., McNeil, Christopher J., Wells, Ralph F. 1973. Clindamycin-Associated Colitis. Journal of the American Medical Association. 223:1379-1380.
- Davis, John C. 1974. Severe Colitis Following Lincomycin and Clindamycin Therapy. The American Journal of Gastroenterology. 62:16-23.
- Dearing, William H., Baggenstoss, Archie H., Weed, Lyle A. 1960. Studies on the Relationship of Staphylococcus Aureus to Pseudomembranous Enteritis and to Postantibiotic Enteritis. Gastroenterology. 38:441-451.
- Ecker, Jerome A., Williams, Robert G., McKittrick, James E., Failing, Robert M. 1970. Pseudomembranous Enterocolitis--An Unwelcome Gastrointestinal Complication of Antibiotic Therapy. The American Journal of Gastroenterology. 54:214-227.
- Fekety, Robert F. 1968. Gastrointestinal Complications of Antibiotic Therapy. Journal of the American Medical Association. 203:144-146.
- Geddes, I. M., Bridgewater, F. A. J., Williams, D. N., Oon, J., and Grimshaw, G. J. 1970. Clinical and Bacteriological Studies with Clindamycin. British Medical Journal. 2:703-704.
- Georgopoulos, Basil S. and Chrisman, Luther. 1970. The Clinical Nurse Specialist: A Role Model. American Journal of Nursing. 70:1030-1039.
- Goodacre, R. L., Hamilton, J. D., Mullens, J. E., and Qizilbash, A. 1977. Persistence of Proctitis in 2 Cases of Clindamycin-Associated Colitis. Gastroenterology. 72:149-152.
- Goodman, L. S. and Gillman, A. Z. 1970. The Pharmacological Basis of Therapeutics. Ed. 4 New York, The Macmillan Co.
- Goth, Andres. 1976. Medical Pharmacology. Ed. 8 Saint Louis The C. V. Mosby Co.
- Goulston, S. J. M. and McGovern, V. J. 1965. Pseudo-Membranous Colitis. Gut. 6:207-212.

- Groll, A., Vlassembrouck, M. J., Ramchand, S., and Valberg, L. S. 1970. Fulminating Noninfective Pseudomembranous Colitis. Gastroenterology. 58:88-95.
- Hakkal, Halappa G. 1974. The Radiology Corner* Pseudomembranous Colitis Associated with Antibiotics. The American Journal of Gastroenterology. 78-82.
- Howard, Ernest B. 1973. AMA Drug Evaluations. Ed. 2 Acton, Mass. Publishing Sciences Group, Inc.
- Jackson, B. T. and Anders, C. J. 1972. Idiopathic Pseudomembranous Colitis Successfully Treated by Surgical Excision. British Journal of Surgery. 59:154-156.
- Kaplan, Kenneth and Weinstein, Louis. 1968. Lincomycin. Pediatric Clinics of North America. 15:131-139.
- Katz, L., LaMont, J. T., Trier, J. S., Sonnenblick, E., Broitman, S. A., and Rothman, S. W. 1977. A Model of Clindamycin Associated Colitis in Rabbits. Gastroenterology. 72:1078.
- Koltz, Arthur P., Palmer, Walter L., and Kirsner, Joseph B. 1953. Aureomycin Proctitis and Colitis: A Report of Five Cases. Gastroenterology. 25:44-47.
- Manashil, Gordon B. and Kern, Jay A. 1973. Nonspecific Colitis Following Oral Lincomycin Therapy. The American Journal of Gastroenterology. 394-399.
- Pettet, Jacqueline D., Baggenstoss, Archie H. Dearing, William H. and Judd, Edward S. 1954. Postoperative Pseudomembranous Enterocolitis. Surgery, Gynecology and Obstetrics. 98:546-552.
- Pittman, Fred E., Pittman, Joan C., and Humphrey, Charles D. 1974. Colitis Following Oral Lincomycin Therapy. Archives of Internal Medicine. 134:368-372.
- Ramirez-Ronda, Carlos H. 1974. Incidence of Clindamycin-Associated Colitis. Annals of Internal Medicine. 81:860.

- Reiner, Leopold, Schlesinger, Monroe, and Miller, Gerald. 1952. Pseudomembranous Colitis Following Aureomycin and Chloramphenicol. A.M.A. Archives of Pathology. 54:39-67.
- Reiter, Frances. 1973. Improvement of Nursing Practice. Cited in Reihl and McVay, The Clinical Nurse Specialist. Ed. 1 New York, Meredith Co.
- Riehl, Joan and McVay, Joan W. 1973. The Clinical Nurse Specialist. Ed. 1 New York, Meredith Co.
- Schapiro, Rolf L. and Newman, Arnold. 1973. Acute Enterocolitis. A Complication of Antibiotic Therapy. Diagnostic Radiology. 108:263-268.
- Scheibe, O. and Teubner, E. 1968. Antibiotic-colitis. The American Journal of Proctology. 19:353-356.
- Scott, Alister J., Nicholson, Gordon I., and Kerr, Alan R. 1973. Lincomycin as a Cause of Pseudomembranous Colitis. The Lancet. 2:1232-1234.
- Sinatra, Frank, Buntain, William L., Mitchel, Charles H., and Sunshine, Philip. 1976. Cholestyramine Treatment of Pseudomembranous Colitis. The Journal of Pediatrics. 88:304-306.
- Sleisenger, M. H. and Curtis, K. J. 1973. Infectious and Parasitic Diseases. Cited in Gastrointestinal Disease. Philadelphia. W. B. Saunders Co. 1369-1373.
- Spiro, Howard M. 1970. Clinical Gastroenterology. Toronto. The McMillan Co. 397-399.
- Summer, Hatton W. and Tedesco, Francis J. 1975. Rectal Biopsy in Clindamycin-Associated Colitis. Archives of Pathology. 99:237-241.
- Tedesco, Francis J., Barton, Robert W. and Alpers, David H. 1974. Clindamycin-Associated Colitis. A Prospective Study. Annals of Internal Medicine. 81:429-433.

- Tedesco, Francis J., Stanley, Robert J., and Alpers, David H. 1974. Diagnostic Features of Clindamycin-Associated Pseudomembranous Colitis. The New England Journal of Medicine. 190:841-843.
- Tedesco, Francis J., Anderson, Charles B., and Ballinger, Walter F. 1975. Drug-Induced Colitis Mimicking an Acute Surgical Condition of the Abdomen. Archives of Surgery. 110:481-483.
- Terplan, Kornel. 1953. Fatal Fulminating Staphylococcic Gastro-Enterocolitis with Shock-Like State Following Antibiotic Treatment. American Journal of Pathology. 29:595-596.
- Theodoropoulos, G., Seitanidis, B., and Archimandritis, A. 1975. Clindamycin-Associated Colitis: Report of a case. Disease of the Colon and Rectum 18:436-437.
- Tully, Timothy E. and Feinberg, Samuel B. 1974. A Reappearance of Antibiotic-Induced Pseudomembranous Enterocolitis. Radiology. 110:563-567.
- Valberg, L. S. and Truelove, S. C. 1960. Noninfective Pseudomembranous Colitis Following Antibiotic Therapy. American Journal of Digestive Diseases. 5:728-737.
- Viteri, Alfredo L., Howard, Paxton H., and Dyck, Walter P. 1974. The Spectrum of Lincomycin-Clindamycin Colitis. Gastroenterology. 66:1137-1144.
- Wagner, J. G., Novak, E., Patel, N. C., Chidester, C. G., and Lumis, W. L. 1968. Absorption, Excretion and Half-Life of Clinimycin in Normal Adult Males. The American Journal of the Medical Sciences. 256:25-37.
- _____. 1971. Forms of Colitis. British Medical Journal. 698-699.
- _____. 1975. Antibiotic Diarrhoea. British Medical Journal. 5991:243-244.