5-1-1938

Chronic ulcerative colitis of a familial nature

Donald W. Miller
University of Nebraska Medical Center

CHRONIC ULCERATIVE COLITIS
OF A FAMILIAL NATURE

By

Donald W. Miller

Senior Thesis Presented
To the College of Medicine,
University of Nebraska,
Omaha, 1938.

PREFACE

In southwestern Nebraska there has dwelled a family harrassed by a most belligerent and bellicose disease which insidiously afflicts one by one each member of the family. At the present time the father and four children have been or are troubled, three children have died, and only three out of the family of ten children are well. In each case the manifestations are similar in character, and either the disease runs on with diabolical progression, or ends in temporary remission. But with remission this black cloud continues to hang over the head of these people, for they do not know when it will again recalcitrate with an acute recrudescence that will cast them into a bedridden, "skin and bone" shadow of their former selves.

Several of them have been to numerous doctors and to some of our better hospitals including the Mayo Hospital and the University of Nebraska Hospital, but, although some have improved, they have suffered exacerbations or are hoping against fate that they will not again be subjected to the anquish of this devastating impregnable disease.

It is therefore my objective in this paper to present this family and its disease in its entirety,

so that in the future the medical profession can understand more completely the malady with which it is dealing, and be better equipped to institute adequate, expedient treatment for those that are afflicted and afford prophylaxis for those that are not. Since some pertinent factor may have hereto-fore been overlooked, the family history will be presented in considerable detail and will be considered from all possible angles in an effort to disclose the exact nature of the process.

For this presentation the family has been kind enough to allow me to use their names, but for any future reference I must request that the names of the family, as well as the doctors that treated them, be omitted.

THE TILSE FAMILY

The Tilse Family is a hardy group of people that consist of a living Father and Mother and ten children of whom three are dead and seven are living. They have been reared on various farms in western Nebraska until 1918 and since then have lived at Cambridge, Nebraska. They have been a hard working group of people that have spent many long days in the fields on their farm and even some of the girls worked in the fields side by side with the men. They are all energetic and, although they began relying on their own initiative at a very young age, varying from seventeen to twenty-three, several of them managed to put themselves through one or more years of college at Greeley, Colorado. However, most of them have been hampered by periods of invalidism due to colon trouble.

The Father is seventy-four and now is in somewhat of a senile dementia and has been gruff and cranky with his family. Due to his mistreatment of the children they all left home early in life. The mother, age sixty-three, is a large, fleshy, buxom woman that is quite opinionated, but she has always been good to the children. The children in order of their birth are

Willie Tilse, Marie Tilse, Anna Tilse, Clara Tilse, L. H. (Dutch) Tilse, Albright Tilse, A. W. (Pat) Tilse, Leonard Tilse, Arnold (Alex) Tilse, and Irene Tilse. Three of the children, Irene, Albright, and Clara, have always been well; three of them, Willie, Marie, and Leonard, are dead; and all of the rest have been troubled to a greater or lesser degree with intestinal trouble.

There is no antecedent familial history other than that of an Uncle on the mother's side by the name of Fritz Klinge. Little is known of his case except that he was poorly at the age of forty with a diarrhea consisting of blood, mucus, and pus, and that after a few years he again became well and lived to the age of ninety-nine. He never went to a doctor to have a complete examination and it is reputed that he attributed his final salubrity to the use of alcohol. None of the grandparents was ever affected by a disease such as seen in this family and they all lived to an old age, especially the grandparents on the father's side of the house who lived to be eighty-nine and ninety-three respectively. There is no other disease of a familial nature except a history of cancer in Mrs. Reiser, mother of Mrs. Tilse, and in one of Mrs. Reiser's sisters. The former died of cancer of the kidney at the age of sixty and the latter of

cancer, but of unknown type.

The members that have been affected are presented in as much detail as has been available through direct questioning and questionaires sent to all of the different members of the family, and from consultation and correspondence with most of the Doctors who have treated them.

Case 1 Mr. Tilse

Mr. Tilse was born in 1863 and came to this country at the age of twenty-seven. He was perfectly well until the age of thirty-two. At this time he was living with an uncle in Saline County, Nebraska. While with this uncle, he suddenly became troubled with diarrhea consisting of loose frequent movement of pussy stools streaked with blood, and he attributed it to something that he had eaten. The uncle, however, had no such trouble. He was thence bothered intermittently up to the age of sixty-two when he was somewhat relieved by a hemorrhoidectomy, and finally recovered completely. For thirty-one years he had to be careful of his diet, and recurrences were apt to occur following any hard work. He obtained the most relief from eating only bland foods such as scalded milk, and toast, and by taking Baker's Pain Relief Liquid. He is five feet eleven inches tall and at present weighs

one hundred sixty-five pounds, which is thirty pounds more than he weighed during his attacks of diarrhea, but thirty pounds less than his best weight.

Case 2 Mrs. Tilse

Mrs. Tilse has never had any blood in her stools, but throughout her life she has been bothered occasionally with short periods of constipation and short periods of diarrhea. Sometimes there was some associated abdominal griping pain, but she didn't lose any weight and has never been troubled more than a day at a time.

Case 3 Willie Tilse (1899-1913)

Willie Tilse was well until March, 1911 when, at the age of twelve, in a weak and depleted condition from hard work cultivating corn in the farm fields, he began to complain of abdominal distress and short periods of diarrhea. These periods were preceded for a few weeks by obstinate constipation, and the diarrhea lasted only about six or eight days. It consisted of six to twelve milky, yellow colored stools a day containing blood, mucus, and pus and these were of slightly greater frequency during the day. He vomited occasionally and suffered

griping pain in his abdomen along with tympanities and tenesmus. The pain was located over the descending colon. Bulky foods, acid foods, and condiments aggreviated his condition and he could eat only bland foods such as eggs, cheese, rice, and Horlick's Malted Milk.

He improved somewhat during the winter 1911-1912, but following a cold in the spring he suffered a recrudescence and from then on gradually lost weight, became extremely emaciated, and died in August, 1913.

He also had had a skin eruption that was diagnosed as psoriasis by Dr. Marsteller of Wilcox, Nebraska. It consisted of dry scaly lesions that itched and were scattered over his entire body. These had been present long before the onset of his intestinal complaint and were present the year around.

Dr. Marsteller, who is now deceased, believed the condition to be a low grade of typhoid fever. Dr. Rogers of Ragan, Nebraska later called it colitis and treated it with enemas, milk of magnesia, and a bland diet including Horlick's Malted Milk. However, to the families knowledge no X-rays or proctoscopy were done.

Case 4 Marie Tilse (1900-1933)

Although Marie Tilse had occasionally been troubled with obstinate constipation, at the age of eighteen she began to suffer from an exuberant diarrhea consisting of blood, mucus, and pus. She complained of pyrosis and vomited occasionally. Associated with this were severe attacks of pain located on both sides of her abdomen. These varied from dull griping pains to frequent, poignant, excruciating pain. Condiments, beets, corn, cabbage, and other bulky food in the diet enhanced the pain while soft foods and liquids seemed to give her some relief. She was frequently flatulent and suffered from tenesmus. Her best weight was one hundred and twenty-five pounds, but with the attacks inanition was grave and she weighed only ninety to one hundred and ten pounds.

She saw Dr. Rogers of Ragan, Nebraska while in an acute stage and he called it appendicitis and prescribed a tonic. In 1919 she saw Dr. Kee of Cambridge who operated for appendicitis. She experienced a stormy convalescence, however, and had to remain in the hospital for three months, after which her condition was unimproved. She then tried osteopathic treatments with no results.

Finally she went to the Mayo Clinic in December, 1922. When seen at Rochester(Logan, Arch H.: Personal correspondence), she was badly emaciated and weak, and

ahe had a marked anemia, the hemoglobin being twenty-eight percent and the erythrocytes numbering 2, 830,000. Because of a questionable lesion in the right upper lobe, the sputum was examined for the tuberculous bacilli, but none was found. Also, two examinations of the stools for Mycobacterium Tuberculosis were negative, and there were no ova, parasites, or cysts. Proctoscopic examination showed a pale mucosa that was easily traumatized, but very little ulceration. The lumen was contracted about one third up to the third valve of Houston, and just beyond this the bowel angulated anteriorly and further examination was difficult. It was seen, however, that the sigmoid was contracted to less than one centimeter in diameter.

The diagnosis was chronic ulcerative colitis and after giving her transfusions, a Brown ileostomy was done. The ileum was severed four or five inches above the ileocecal valve and both ends were brought out through the abdominal incision. Following the operation she contracted influenza and bronchitis, but after these cleared up she began to gain in weight and strength.

She returned to the Clinic in August 1924, however, because of prolapse of the bowel through the ileostomy wound. Stool examinations showed no Bargen diplostrepto-

coccus or parasites. At this time a proctoscopic examination showed the bowel to be contracted more than formerly; the lumen of the rectum was about two-thirds centimeter, and the sigmoid one centimeter in diameter. She also had an anal fissure and a few external hemorrhoidal tabs. In September, 1924 some plastic surgery was done on the malfunctioning ileostomy. This was again unsatisfactory and a partial resection of the ileum was done. Following this she improved and became quite well.

She returned for the last time in December, 1929, because of continued recurring rectal discharge and distress and she hoped that further surgery might be performed to relieve her. Her hemoglobin was twelve and one half grams, and the erythrocytes numbered 5,020,000. However, the risk of operation seemed too great to consider a colectomy at that time. The colon was so contracted this time that proctoscopic was impossible.

She continued to have recurrent recrudescences from this time on and in 1933 she died of a perforation resulting in peritonitis.

Case 5 Anna Tilse

Anna Tilse was born March 30, 1901. She was married in 1930 and has lived on different farms in southwestern Nebraska until recently, but now lives at Scottsbluff, Nebraska.

Although she had neither been home nor around anyone of the family who was being troubled with diarrhea, she began to suffer from an occasional attack of intestinal trouble two years ago, in 1936. This consisted of a griping pain located low in her abdomen which was followed by a diarrhea of three to five stools per day consisting of non-formed feces streaked with blood and mucus, but no pus. These attacks lasted for one or two weeks. In between such attacks she had a rather contumacious constipation which necessitates her taking laxatives.

Such periods have continued intermittently to the present time and she now has hemorrhoids that have never been treated and which bother her at times. She also complains of a skin eruption which appears about every spring, and consists of large red blotches with white scales. She has had these recurrently since she was eight years old.

Her present diet consits of various types of meat one or two times each week, potatoes, beans, rice, corn,

and other vegetables, oatmeal, eggs, milk, canned fruits, and in the summer months plenty of green vegetables.

Her trouble has never been severe enough so that she has gone to a doctor.

Case 6 L. H. Tilse

L. H. Tilse was born in 1903, and was well until the age of twenty-four, in 1928, when he became thin and overworked with symptoms of general malaise. From this time on whenever he rode tractors he would get severe cramps in both lower quadrants of his abdomen. He would become bloated and borborygmus sounds were audible. During these periods he suffered rectal tenesmus and there was a mild diarrhea with associated copious gas, but there was never any blood. There was no associated fever or residual soreness between cramps.

These symptoms gradually became worse so that in 1932 he had frequent recurring attacks with at least three severe ones. Three to four hours following his meals he would develop severe cramps in his abdomen, he would become tympanitic and distended, and occasionally at the height of the pain he would vomit. After his bowels were emptied he was relieved and as long as he ate a soft diet he remained fairly well. Finally, in May

1932, he became so ill that he would frequently have to fast for two or three days before being relieved of his pain and , consequently, he lost sixteen pounds in weight.

June 16, 1932, he went to see Drs. W. W. Arrismith(2), W. J. Arrismith , and A. P. Synhorst (107) of Grand Island. They diagnosed the condition as some form of obstruction and operated June 19, 1932. A low mid line incision was made and exploration revealed a mass involving the lower ileum about five feet from the ileocecal valve. This mass was almost obstructing the lumen of the bowel. Above the mass the bowel was markedly dilated and hypertrophied. For a distance of approximately three feet the bowel below the mass was contracted and of a deep reddish-brown color. An occasional enlarged lymph gland was found in the mesentery. The remaining portion of the small bowel and thelarge intestine appeared normal. The appendix was of the obliterating type and bound retrocecally by an anatomical membrane. There were no enlarged glands along the aorta. Approximately fifty inches of the lower ileum was resected and an end to end anastomosis made.

On opening the bowel after operation an opening about the size of a lead pencil was found at the proximal end

where the mass involved the bowel. Below this for approximately the entire distance of the resected portion of the bowel the mucous membrane was destroyed and replaced by a peculiar, irregular growth through-out its entire extent. There was normal mucosa for a distance of four or five inches on either side of the diseased tissue.

This tissue was sent to the pathology department of Harvard Medical School. On examination they found numerous abscesses in a greatly thickened submucosa. These appeared as a more or less indolent type in which lymphoid cells and mononuclear phagocytes predominated. Only the very centers of the abscess contained enough polynuclear leucocytes to indicate puriform softening. Some of them were surrounded by early granulation tissue, and a few contained giant cells. These abscesses communicated with the surface through minute ulcerations which were in evidence.

The only microorganisms which could be identified were large bacilli in colony form. The type of suppuration corresponded in general to that caused by the gram negative bacilli of the colongroup and Friedlander's Bacillus groups. The great thickening of the gut was caused by a fairly widespread edema, lymphocytic infiltration, and

fibrosis chiefly in the submucosa, but also present in the subserous coat and the mucosa itself.

The lesions did not spread laterally. Each one seemed to be an independent lesion taking origin by invasion from the lumen of the gut.

Following this operation the patient gradually recovered and gained weight and has not been troubled since. He now weighs more than at any time and eats a perfectly normal diet with no trouble at all.

Case 7 Albright William Tilse

Albright Tilse was well until the latter part of August, 1936 at which time he began to be troubled with sharp pains in his rectum associated with bowel movements. He noticed blood in his stools and thought he had piles so he went to Dr. P. W. Tipton who found hemorrhoids and performed a hemorrhoidectomy. During the operation Dr. Tipton discovered an abscess inside the rectum. A week later the abcess broke and he then began to improve. However, this improvement did not last long as he soon began to have a profuse diarrhea of as many as twenty to twenty-five stools a day, and he was therefore sent to the Covanent Hospital October 28, 1936. At this time the stools were a thin liquid varying in color

from a yellow to a dark brownish-green, and contained blood, mucus, and pus, but were not frothy or accompanied by very much gas. He complained of griping abdominal pain along the colon and vomited as often as two or three times a day.

Previous to this time he had worked as a farm laborer, a truck driver, and a service station operator. The past two years he had worked as a truck driver between Chicago and Omaha. For the past five to seven years he had eaten at resturants throughout the midwestern part of the United States, chiefly in Colorado, Nebraska, Iowa, and Illinois. He generally ate two times per day and his diet consisted of the usual restaurant diet of meat , vegetables, fruits, potatoes, bread, coffee, and very rarely green vegetables.

Laboratory examination at the Covenant Hospital revealed:

Blood (10-28-36): RBC--4,600,000
Hb---85%
WBC--10,800

Urine: Negative

Blood Agglutinations: Typhoid---------Negative
Undulant Fever--Positive
in 1:40 dilution.

Stool examinations added information as follows:

10-28-36 No parasites, amoeba, or cysts found.

10-29-36 Amoeba present of atypical type. The amoeba was a sluggishly motile protozoa, but in a field of many red blood cells contained only a few red blood cells.

11-3-36 Blood streaked mucous stool with amoeba present.

On the strength of this laboratory report treatment was instituted as follows:

1. 1:5000 acriflavine enemas,

2. Tincture of opium and bismuth aa dram 2 every two hours,

3. Emetine hydrochloride by hypo---gr ½ per day, and later carbarsone also was tried,

4. Paregoric by mouth and analgesics, namely sodium luminal, and sodium amytal, as needed.

The patient stayed in the hospital from October 28 to November 21 when he was transferred to the University of Nebraska Hospital. During this time there was very little improvement in his condition.

Thus at the time of admission to the University of Nebraska Hospital he was having a diarrhea of liquid stools containing blood, mucus, and pus with much rectal tenesmus and abdominal griping pain. He had lost sixty pounds of weight, weighing only ninety-nine pounds while

his normal weight was one hundred sixty pounds, and four or five days prior to entrance he began vomiting more severely than he had previously.

Physical examination revealed a badly emaciated male and was otherwise irrelevant. He had no glossitis and his blood pressure was 120/70 with a rapid pulse but with normal heart tones.

Rectal examination showed an atonic sphincter with a buldging of the rectum just above the prostate suggestive of a draining pelvic abscess, and a large firm, ulcerated mass located near the upper part of the rectum.

Anoscopic at this time showed a large edematous mass in the rectum about the size of a golf ball located four or five inches above the anal ring. This mass was ulcerated with firm raised edges and presented a somewhat cauliflower-like appearance. A biopsy was taken with the radio-knife, and smears taken for iron hematoxylin stains. Microscopic study of the biopsy material did not show malignancy, but that the specimen consisted only of inflammatory tissue with ulceration of the mucosa and leucocytic infiltration. No parasites could be identified with the tissue or in the smears.

Proctoscopic gave a picture of marked edema of the mucosal walls with numerous ulcerations and necrotic areas.

Small polypoid protruberances projected from the walls of the bowel, but there was so much edema and purulent discharge that the degree of ulceration and polyposis could not be clearly determined.

Laboratory examination contributed as follows:

Blood: RBC--3,100,000
Hb---65%
WBC--8,000
Differential--Seg---------45
Staff-------33
Young-------- 9
Lymph-------- 9
Mono--------- 2
Myel--------- 1
Plasma Cell- 1

Stools: Repeated examinations showed no amoeba, ova, or cysts. Smears revealed no acid fast organisms and contained chiefly gram negative bacilli. Cultures grew B. Coli, B. Typhosus, and Paratyphosus B.

Proctoscopic smears from the ulcers contained no amoeba, no acid fast bacilli, but did contain many pus cells, and gram negative bacilli.

X-ray (FigureI) of the abdomen showed some slight enlargement of the liver. Barium enema revealed a gross irregularity of the upper rectal ampulla giving the appearance of a papillary proliferation of tissue. The transverse colon showed irregular serations in contour such as are commonly seen in amoebic dysentery or in

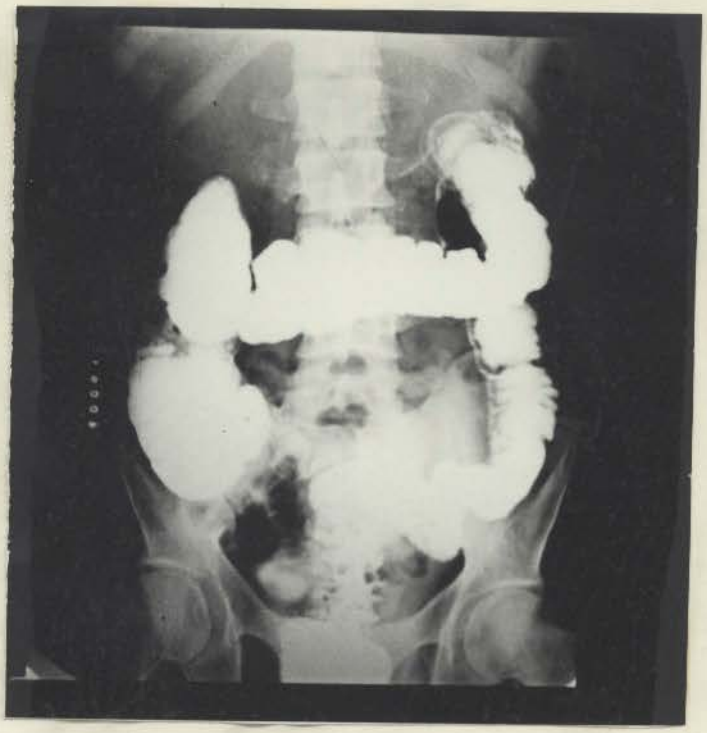


FIGURE I
Roentgenogram of A. W. Tilse (12-22-36)

atypical chronic ulcerative colitis. There was no gross deformity of the cecum evident.

On admission the treatment given the patient included:

1. A low residue,high caloric, high vitamin diet,

2. Bismuth subcarbonate gr. 20 t. i. d. by mouth,

3. Chiniofon gr. 4 q. i. d. by mouth and chiniofon oz. 6 of 1% solution per retention enema,

4. Acriflavine gr. ½ t. i. d. by mouth and acriflavine 1:5000 solution oz. 6 per retention enema,

5. Reduced iron gr. 10 t. i. d., and

6. Elixir I. Q. S. oz. 1 t. i. d.

The chiniofon was stopped at the end of a week and yatren tab 1 t. i. d. and yatren per rectum were used in its place. Paregoric and milk of bismuth were added by mouth along with hot packs to the abdomen t. i. d. On 12-16, the yatren was stopped and the patient was put on two way rectal irrigation with 1:5000 KMNO4 solution via an inflow and outflow catheter. Later cod liver oil retention enemas were tried.

There was little improvement for some time. Gradually, however, the ulcerated polypoid mass in the rectum decreased in size and became less inflammed revealing a concavity in the anterior wall of the rectum that drained free pus. This was in the former location of the suggestive buldging mass. Likewise the ulceration and edema of the bowel gradually subsided following the irrigations with KMNO4 and the cod liver oil retention enemas so that proctoscopic on 1-6-38 revealed a much improved mucosa with only a small amount of residual inflammation and the ulcers were considerably improved. Many

polyps were present and appeared to be of the type that follows secondary inflammation rather than the congenital type. He then continued to improve so that he was dismissed February 12, 1937.

Since that time he has gained weight, until at present he weighs 165 pounds and is able to eat almost any type of food. Although he occasionally has pains in the colon and rectum that last a day or so and then disappear, he has otherwise been entirely free from symptoms.

He had been away from home for eight years before the onset of this trouble, and, during that time had not associated with any of the members that were ill, so could not have obtained the disease from his family.

Case 8 Leonard Tilse

After having been away from home for one year, Leonard Tilse began to suffer from periodic gastro-intestinal upsets with nausea, and vomiting and a watery diarrhea. While attending school at Greely, Colorado, flatulence and tenesmus accompanied these attacks and an intermittent, spasmodic, abdominal pain was associated with the nausea and vomiting. At first he thought it due to eating a bad hamburger, but these attacks became more frequent, he became weaker, and he progressively lost

weight. Finally, in 1932, the periods of diarrhea became more frequent, and consisted of large amounts of mucus and small amounts of blood mixed with a liquid, watery stool. The duration of these attacks was from one to three weeks and nausea and vomiting were concomitant with them. He had to be careful of his diet and eat only soft bland foods as rough or poorly cooked foods seemed to either initiate or aggreviate the condition.

Finally, discouraged by the results obtained from local physicians, he went to the Mayo Clinic in November, 1934 (Logan, Arch H.: Personal correspondence). At this time laboratory examination disclosed a normal urinalysis, and erythrocyte count of 4,540, 000 with a hemoglobin of 13.9 grams, a leukocyte count of 11,000, and a stomach acidity of thirty-eight degrees total, and twenty-four degrees free following a seventy-five cc. test meal. X-ray of the stomach, colon, and terminal ileum were negative. The diplostreptococcus of colitis was found in the stools, but no ova, cysts, or parasites were present. Proctoscopic revealed an essentially normal mucosa except that the mucosa of the lower sigmoid bled easily upon slight trauma. He was given a soft bland diet and Bargen's vaccine and serum, and after three weeks in the hospital was somewhat improved.

Shortly following his dismissal he began to be troubled with hemorrhoids which caused him considerable pain and prolapsed with defication, but his intestinal trouble was quiescent for a short while. However, recrudescence soon occurred and he continued to be periodically afflicted with symptoms similar to those before.

During the summer of 1936 he became very bad. His local doctor gave him amoebic treatment with no improvement and finally August 21, 1936 he came to the University Hospital. At this time he weighed only one hundred twelve pounds which was fifty-three pounds less than his usual weight of one hundred sixty-five, and his symptoms were weakness, diarrhea of bloody, mucous stools, tenesmus, griping abdominal pain, and nausea and vomiting. He had a skin eruption consisting of several brownish macules on his abdomen and legs of about three or four centimeters in diameter, and several red, pea sized papules covered with a silvery, whitish imbricated scale which were located on his arms and were associated with brownish macules similar to those on the abdomen and legs. A diagnosis of psoriasis was made and it was treated with sunlight, ultra violet light, and a prescription of 6-12% resorsin and 2% salicylic acid in an ointment base.

His abdomen was tender throughout to palpation and his blood pressure was 108/68; his joints were stiff, but not painful. Rectal examination revealed three large external hemorrhoids and an opening anterior to the anus discharging a whitish exudate.

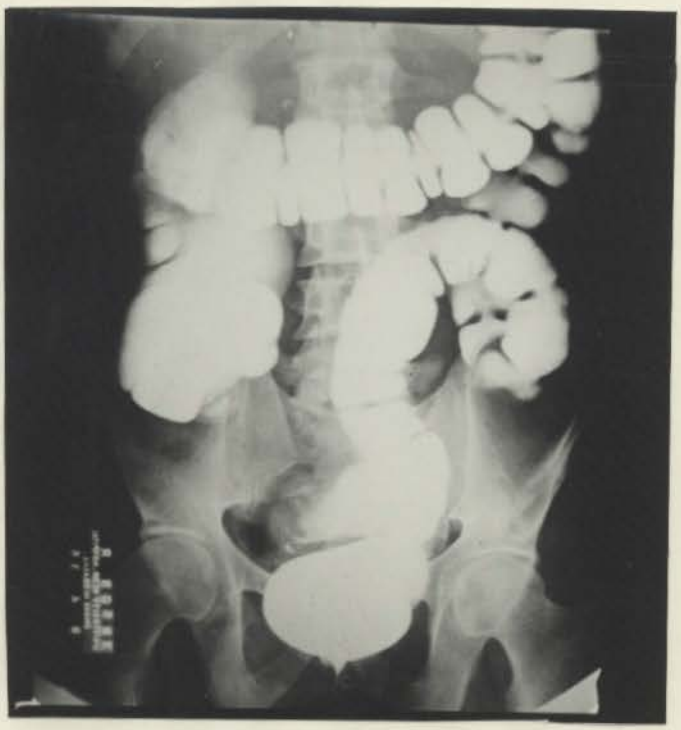


FIGURE II
Roentgenogram of Leonard Tilse (September, 1936)

Proctoscopic examination revealed a pale, granular, edematous mucosa which bled easily upon manipulation. There were no ulcers, but there were a few small ecchymotic, hemorrhagic points.

Roentgenology with a barium enema showed a redundant loop in the sigmoid region, but there was no apparent narrowing of the descending colon or upper rectum to suggest a hyperplastic thickening of the colonic wall which occurs in long standing cases of ulcerative colitis.

Laboratory examination revealed:

Gastric: Free acidity of 78 and a maximum total of ninety degrees.

Blood: Hb--70%
RBC-4,119,000
WBC-4,800

Stool examinations:
8-25-36 Liquid light yellow stool with no parasites, ova, or cysts.

8-26 and 27-36 No ova, cysts, or parasites.

8-25-36 Brain Broth Culture, revealed gram negative and gram positive bacilli, a few lancet shaped diplococci suggestive of Bargen's Diplococcus. Endos culture showed B. Coli.

8-27-36 Culture in brain broth, on blood agar plates, and on endos medium revealed B. Coli.

Blood Chemistry:
Total serum protein-3.5 mg. per 100 cc.
Serum albumin-------1.3 mg. per 100 cc.
Serum globulin------2.2 mg. per 100 cc.
Blood Calcium-------8.5 mg. per 100 cc.

He was placed on a regime consisting of:

1. A high caloric, high vitamin, low residue diet;

2. Ryzamine B;

3. Bed rest;

4. Calcium carbonate, bismuth subcarbonate, calcium phosphate--aa dram every four hours; and,

5. Bargen's serum 1.5 cc. daily.

On this treatment he gradually improved, gained weight, and his diarrhea diminished so that he was dismissed October 5, 1936.

After leaving the hospital he was all right for about two weeks, but then went into a severe exacerbation with added symptoms of swelling of his eyes and feet. He went to a local hospital and was given amoebic treatment but with no avail. The swelling of his legs continued to get worse, his diarrhea was augmented, and he weighed only ninety-five pounds. Consequently, he returned to the University Hospital February 16, 1937.

His laboratory findings revealed a decrease in normal serum consitutents, and his anemia was more sever e.

Laboratory data was as follows:

Blood: RBC----------3,800,000
Hb----------65%
WBC----------4.900
Hb Concentration----------33.6%
Mean Corpuscular Hb--------29rr
Mean Corpuscular Vol. -----85.5 Cu U
Differential-- Segs---30
Staff--40
Lymph--24
Mono----3
Young-- 3

Stools: Occult blood-positive
No amoeba, cysts, or parasites seen.

No Bargens diplococcus. Stool contains large amounts of fat and were frothy and doughy in consistency.

Blood chemistry:

Serum cholesterol	170 mgm%
Blood sugar	86 mgm%
Serum protein	3.3%
Serum albumin	1.5%
Serum globulin	1.8%
Blood calcium	7.7mgm%.

Physical findings were as before with the addition of a reddened, bauld type of glossitis.

He was given:

1. Insulin U 5 t.i.d., to stimulate his appetite,
2. Liver extract---2cc I.M. every second day,
3. Milk of bismuth and paregoric
4. laudanum per retention enema,
5. ryzamine B ---drams 1 t.i.d.,
6. viosterol-----gtts 10 t.i.d.,
7. chinifon -----gr. 4 t.i.d., and
8. emetine hydrochloride---gr ½ per hypo q.i.d.

However the patient continued to decline and died March 19, 1937.

Macroscopically autopsy disclosed that the lower lobe of the left lung and all of the right lung contained several abscess cavities which varied from four centimeters in diameter to microscopic size, and there was also some associated hypostatic congestion. The bowel was collapsed throughout most of its length, and the intestinal blood vessels were greatly dilated. About three feet below the ligament of Treitz the first of a series of constrictions

marked by granularity of the serosa was found. There were numerous fibrous bands which were particularly marked through about four feet of the proximal half of the ileum, and the appendix was shortened and fibrotic. The terminal ileum was greatly thickened and numerous adhesions were found about the cecum. The vena cava was filled with a firm ante-mortem thrombus most of which was firmly attached to the wall, and this extended into the iliac veins of both sides, but was somewhat cannelized in the left iliac vein.

The bowel revealed normal gastic mucosa, but the duodenal mucosa was hemorrhagic, extremely granular in appearance, with one or two tiny areas of ulceration. The mucosa of the jejunum was necrotic with several sharply circumscribed ulcers one centimeter in diameter and the upper ileum showed similar ulcers some of which were more linear in form. A few inches farther down the ulcers became much larger and irregular in outline, they frequently encircled the walls, and the walls, themselves, were composed of fibrous tissue, with only a few islands of mucosa. The edges of the ulcers merged with the surrounding epithelium. More distally the ulceration became continuous and persisted for about two feet. The distal half of the ileum was practically free of ulceration or scarring, and, although the mucosa of the colon appeared

to be somewhat thinner than normal, no scars or ulcerations were present.

Microscopically, the peritoneum over the small intestine was thickened and edematous. The muscle layers contained a round cell infiltration and engorgement of the blood vessels. The submucosa was edematous and also had a round cell infiltration and in some areas a leukocytic infiltration. In places the mucosa was entirely absent, while in others it was thinned showing necrosis, hemorrhage and sloughing. Many goblet cells were present. The colon disclosed engorgement of the blood vessels but no tissue necrosis or ulceration. There was an increase in interstitial connective tissue beneath the mucosa.

The postmortem diagnoses were, 1. multiple lung abscesses, 2. thrombosis of the iliac veins, and 3. nontropical sprue which was made chiefly by an exclusion process.

Case 9 Arnold T. (Alex) Tilse

In 1926 while still living at home, Alex Tilse, then 14 years old, began to suffer from an occasional five minute period of nauseating abdominal pain, of such a poignant nature that he would prespire profusely, and would double up in an attempt to get relief.

Concomitantly with these attacks, he had a diarrhea which lasted for two to three days, and towards the end he would become nervous and weak although he was never so sick that he had to go to bed. A pertinaceous constipation troubled him between these periods.

He continued to have similar distress until 1932 when he was 20 years of age. He had been working very hard and obtaining inadequate sleep from 1931-1932 while he was attending Greeley College. He went to school during the day, worked at a filling station at night, and studied whenever he wasn't otherwise busy, so that he obtained only about six hours of sleep daily. Furthermore, he ate irregularly and sometimes his diet was inadequate.

Finally in March, 1932 he suffered from a severe attack of diarrhea, abdominal distress and vomiting which he thought was due to being poisoned from the accidental inhalation of carbon monoxide gas. He was sick for about two weeks, but finally improved. In July of the same year he had a similar attack while working in an automobile paint shop. He lost weight rapidly, lost his appetite, and had a distressing diarrhea of six to eight bowel movements daily accompanied with much gas. The stools were frothy and contained small amounts of blood and mucus. This continued for about five weeks,

but again he gradually improved.

In December, 1932 he became ill with rheumatism which involved his knees, ankles, elbows, wrists, and hands. The joints were swollen, red, and painful, and it moved about from one joint to another in a "dodging manner". Concomitantly, he had a fever and his abdominal pains and diarrhea became worse. He had a frequency of eight to ten movements daily with much gas and the stools were of a very pungent odor. He consulted Dr. Schoen of Greeley, Colorado who suspected a gastric ulcer and prescribed bismuth, a bland diet, and put him to bed for four weeks which resulted in good improvement with a gain of ten pounds of weight.

In March, 1933, he moved from Greeley to Grand Island, Nebraska and again worked excessively hard at a job as service station attendent for 10 hours and at another job of operating a gravel pump for an additional four hours each day. Nevertheless, he continued to improve and in November, 1933 he weighed 165 pounds without his clothes.

However, while duck hunting in November, 1933, he fell into a river which was partially frozen and contained a small amount of ice. As a result he developed a sinus infection, coryza, and bronchitis, along with this there was a recurrence of his abdominal distress,

which was accompanied first with a pertinaceous constipation and later a bad diarrhea. His rheumatism returned, alternating periods of diarrhea and constipation continued, and he lost weight rapidly. Also he became very nervous and irritable.

Therefore, he consulted Dr. W. W. Arrismith of Grand Island(2) who diagnosed the condition as colitis and prescribed peptobismal and a bland diet. This gave temporary relief, but later seemed to augment the distress.

He then went to Dr. E. A. Watson of Grand Island,(113) July 6, 1934. At that time he was having sharp, excruciating stabs of pain in his epigastrium along with some nausea and vomiting, and he was very constipated. The distal one half of the colon was seen to be spastic by X ray. Dr. Watson, thus, diagnosed the condition as chronic spastic colitis associated with nervousness and hyperirritability from the inhalation of gasoline fumes. He suggested that patient might also have been poisoned from the inhalation of tetraethyl lead gasoline fumes which he handled as a service station attendent. He prescribed tincture of belladonaa, saraka(a laxative), and citrocarbonate.

However, the patient failed to improve. The saraka started a diarrhea of eight to ten stools per day which from that time on he was never able to stop. The stools

were frothy, bloody, and pungent, and copious gas accompanied the defication. His abdomen was very sore and tender especially along the descending and sigmoid colon. He had dizzy spells, was weak and easily exhaustible, and he finally became so ill that he was forced to discontinue work in September, 1934.

He then went to Dr. A. P. Synhorst of Grand Island (107) who diagnosed the condition as chronic ulcerative colitis after careful systemic examination including X rays and proctoscopic examination. The proctoscopic revealed a red, edematous, diffusely ulcerated mucosa that was fragile and bled easily. The roentgenograms which were personally seen by this author were very typical of chronic ulcerative colitis. There was some degree of narrowing, shortening, and thickening along with mucosal destruction as shown by haziness and niching of the mucosal border. This was most intense in the rectum and sigmoid and extended to the mid-part of the transverse colon.

Dr. Synhorst advised him to go to the Mayo Clinic, so the patient, therefore, entered the Colonial Hospital at Rochester in November, 1934. At this time proctoscopy (Logan, Arch H.: Personal correspondence) revealed a typical picture of chronic ulcerative colitis with some secondary polyposis and there were two large ulcers 6 X

3 centimeters in the rectum. X ray showed an ulcerative process extending throughout the distal half of the colon. He was anemic as shown by the laboratory findings of an erythrocyte count of 3,980,000, and a hemeglobin of 9.1 grams, he had no free hydrochloric acid in his stomach, and he had hyaline and granular casts in the urine along with a one plus albumin. The stools were composed of pus and blood, but contained neither Bargens diplostreptococcus, nor any ova or parasities. He was treated with serum, a low residue, high caloric, high vitamin diet, and other sundry measures including haliver oil, iron and liver capsules, bismuth powders, lugols solution, brewers yeast, opium suppositories, and normal saline enemas. Under this treatment he improved very nicely and left after three weeks to go the Betts private hospital in Grand Island where he remained four months. By March 1, 1935 he had gained 35 pounds and was doing well.

Dr. E. G. Johnson of Grand Island (56) revised the diet and prescribed enemas containing corn starch, bicarbonate of soda, and powdered alum. These caused very marked irritation and caused a recurrence of the diarrhea. After leaving the hospital he staid in a private home where he had to eat what he could from a general diet, and he gradually became worse, losing weight, and becoming

weak again.

Therefore, in July, 1935 he returned to the Mayo Clinic where it was found that he had an abscess anterior and to the left of the anus with a draining sinus close to the anal margin. Proctoscopic showed numerous discrete, punched out ulcers scattered throughout the bowel with apparently normal mucosa between them and one large ulcer situated on the rectal valve twelve centimeters above the anus. Thus with the general appearance now more like an amebic dysentery, he was given a course of 6 doses of 1 cc of emetin hydrochloride subcutaneously, and this was followed by 12 capsules of carbarsone. However, no ameba were found in his stools. The remainder of the treatment was similar to that given during his previous visit.

He improved and again returned to Grand Island. He went to the Baer Convalescent Hospital for four months andcontinued Bargen serum treatment. He received hot sitz baths for the rectal condition but other fistulae developed at about the rate of one every month. While in the hospital, he was given two overdoses of the vaccine and a severe serum reaction resulted. This seemed to cause a renewal of his colon symptoms and after leaving the hospital in September, 1935 he again gradually became worse. He consulted Dr. Woodruf of Grand Island(119) who

advised that he come to the University Hospital.

He had been eating either at resturants or at private boarding houses for five to seven years, but, since his first visit to Rochester, he adhered as much as possible to a diet such as:

Breakfast----bacon, poached or soft boiled eggs, oatmeal, or cream of wheat, toast, and orange juice.

Lunch-----beef, mutton, or fish boiled, broiled, or roasted, vegetables such as peas, string beans, carrots , beets, and potatoes, and tomato juice.

Dinner----about the same as lunch, fruits such as peaches, pears, apricots, and white cherries, milk, cream butter, white and rye breads, macaroni, rice, and other smooth foods. Deserts such as jello, ice cream, pudding, or custard. All foods were to be as free of excess cellulose as possible.

He entered the University Hospital 3-14-36. His diarrhea consisted of eight to ten pussy, bloody stools per day, he had poor rectal control due to the fistulae, he was troubled with rheumatism, and he had some numbness of his legs and feet. He weighed 112 pounds.

Physical examination revealed that the patient had good teeth, no tonsils, or other foci of infection, a blood pressure of 110/70, tenderness over the entire abdomen especially in the right and left hypochondriums, six fistulae in ano with feces draining from each, and an atonic rectal sphincter. The stools were greenish-yellow in color, watery, and pungent to smell and contained

blood, some undigested food, some mucus, and large amounts of pus.

Proctoscopic revealed typical shallow small ulcers characteristic of ulcerative colitis with diffuse involvement of the membrane. The mucosa was edematous and bled easily.

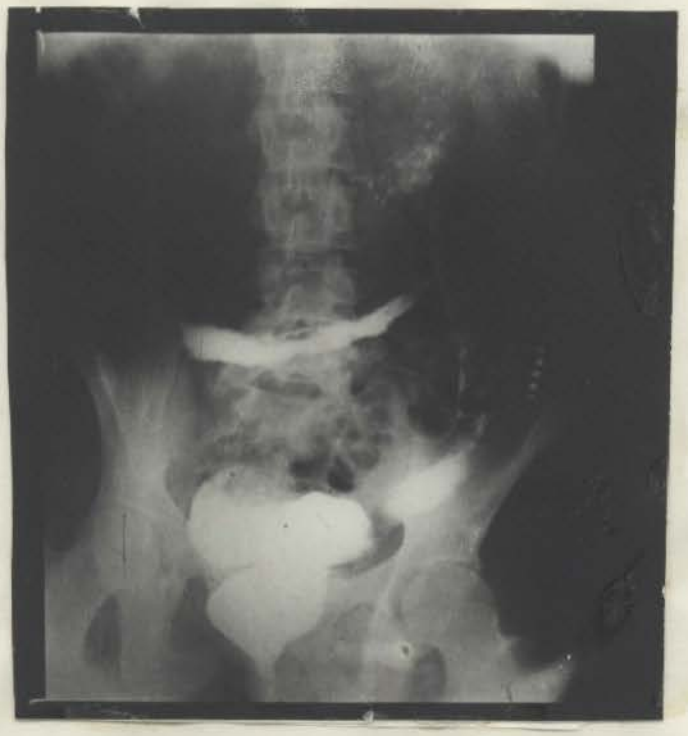


Figure 3: Arnold Tilse roentgenogram, March, 1936

Roentgenology with barium enema showed a slight contracture of the rectal ampulla and narrowing of the sigmoid and descending colon with an absence of haustrations. The walls of the colon were smooth or distorted by fine irregularities consisting of small nodules with intervening

areas of ulceration or pitting.

Laboratory reported information as follows:

Blood:

	3-14 (before operation)	4-15 (after operation)
Hb	75%	65%
Erythrocytes	4,030,000	3,240,000
Leukocytes	17,800	8,300
Segs	45	37
Staff	40	22
Mono	2	3
Lymph	22	29
Young		3
Blast	1	1

Gastric---free acid 46°, total 63°, a trace of occult blood.

Stool examination---four different specimens revealed no ameba, cysts, or ova, and cultures grew B. coli, gram plus cocci, gram plus and negative bacilli, but no Bargens diplostreptococcus. Smears from the ulcers revealed the same as the stools with no typical Bargens diplostreptococcus.

He was placed on luminal--gr 1½, calcium carbonate --gr 20, bismuth subcarbonate--gr 20 five times daily, autogenous vaccine, viosterol--gr 10 t. i. d., reduced iron--gr 10 b. i. d., occasional codeine and morphine, and intravenous glucose 1000 cc. However, he failed to improve with the vaccine therapy, grew despondent and jumped out of the hospital window fracturing his right ulna and radius at the elbow. Due to his poor response to medical treatment an ileostomy was done on 4-9-36. This simply consisted of a temporary tube inserted into the ileum. This proved unsatisfactory so on 4-22-36 a permanent ileostomy was done. Following this he gradually

improved and finally left the hospital in July. He returned to the St. Francis Hospital in Grand Island where he staid for approximately 14½ months, and under the care of Dr. B. R. McGrath of Grand Island he slowly recovered. The ileostomy started to prolapse into the abdomen and had to be reoperated. The rectal fistulae were operated and these also healed nicely. Dr. W. R. McGrath, and B. R. McGrath(83,84) placed him on a medical regime as follows:

1. Amebic treatment --
   Emetine hydrochloride--gr 1 for 10 days,
   Vioform--gr 4 t.i.d. for 12 days,
   Carbarsone---tab. 1, b.i.d. for 12 days.
2. Irrigations of 1:5000 acriflavine, or normal saline once each day,
3. Bismuth subcarbonate and calcium carbonate--aa gr 60.
4. Tincture of opium---minims--- 10 t.i.d.
5. Iron ammonium carbonate in 50% glucose--20 drops t.i.d.
6. High caloric, high protein, non-irritating diet, and
7. Occupational therapy.

Under this treatment the colon discharge which continued for some time, completely stopped and September 3, 1937 he left the hospital weighing 135 pounds.

Since then he has continued to gain weight and strength until he now weighs 148 pounds and eats a fairly normal diet. The ileostomy is working very satisfactorily and there is practically no discharge of pus, mucus, or blood from the colon. He has no abdominal or stomach

distress, no headaches, has lost his nervousness and irritability, and has a good appetite. His strength is improving and he is again working six hours a day.

Case 10 Clara Tilse
Case 11 Albert Tilse
Case 12 Irene Tilse

These three have always been well.

GENERAL DATA CONCERNING THE TILSE FAMILY

The family has lived in Boon County, Nebraska from 1896-1902; Oklahoma for 4 years, 1902-6; at Wilcox, Nebraska for 12 years, 1906-1918; and at Cambridge, Nebraska from 1918 to date. In none of these places has there ever been anyone else in the community that has had any dysentery symptoms. None of their neighbors, who even had occasionally eaten in the Tilse home or had staid at there home during harvest, was ever at all affected.

No one in the family has ever had hay fever, asthma, urticaria, food idiosyncrasies, migraine, eczema, or spasmodic rhinorrhoea.

Their home, although not modern has always been kept very clean, and their diet has been quite adequate. During the summer months they had plenty of green vegetables

and always had plenty of milk. Their usual diet consisted of meat of all kinds with a predominance of pork, potatoes, beens, peas, cabbage, corn, potatoes, eggs, pancakes, cereals, pies, cakes, soup, milk, cream, and other foods.

Their father was not as agreeable as he might have been and made his children work hard even when youngsters. There were frequent quarrels between the father and the sons which resulted in the sons leaving home at an early age, but otherwise their family home life was quite normal.

No member of the family has been exposed to or has had tuberculosis unless it was the daughter Marie and her lung findings at the Mayo Clinic were only suggestive, and were never confirmed by a positive sputum or clinical symptoms. They have had lots of unpasteurized milk, but in recent years all of their cows have been tuberculin tested, and none of their milk cows have ever been positive in these tests. However, in 1925 and 1926 they did have abortion in their dairy herd, but, although they used the milk, none of them ever developed any sickness with the characteristic fever, arthritis, neuralgic pains, or sweating that was not associated with attacks of colitis. None had a splenomeglia either so if any of them have had undulant fever, their infection with the brucella abortus has been very mild.

The disease cannot be considered contagious since four of the family, A. W. Tilse, L. H. Tilse, Leonard Tilse, and Anna Tilse, were attacked by the disease several years after they had been separated from their family. The remainder have either been home or have visited at home shortly before the onset of their trouble, but most of them have lived with afflicted members of the family several years before they, themselves, became ill. Furthermore, neighbors living and associating with the family have never been afflicted.

DIFFERENTIAL DIAGNOSIS

In arriving at the correct diagnosis of the disease producing the diarrhea in this family, the following possible conditions must be considered. These may be classified as follows(4, 11, 71, 88):

I. Ulcerative processes:
1. Chronic ulcerative colitis,
2. Tuberculous colitis,
3. Amebic dysentery,
4. Bacillary dysentery,
5. Typhoid fever.

II. Non-ulcerative processes with organic pathology:
1. Polyposis,
2. Diverticulosis
3. Neoplastic disease---carcinoma, sarcoma, lymphosarcoma,
4. Granulomatous disease--T. B., syphilis, lymphogranuloma, and non-specific.

III. Parasitic infestations:

IV. Disease of systemic origin:
1. Mucous colitis,
2. Nervous diarrhea,
3. Allergic diarrhea,
4. Reflex diarrhea from some other acute infection such as acute appendicitis, acute cholelithiasis, occasionally acute lung involvements, uremia, and acute poisonings.
5. Pellagra,
6. Sprue.

Of these the ulcerative group requires the most attention and is the most difficult to differentiate.

CHRONIC ULCERATIVE COLITIS

Chronic ulcerative colitis is a clinical syndrome which gives a characteristic history(4) of recurrent and intermittent attacks of bloody, purulent rectal discharge of equal day and night frequency which have dated back for a duration of several months. This continues in a depleting course which lasts several years, and, frequently, ends in chronic invalidism.

In the earlier stages of the disease(43, 96, 119, 65), there are periods of alternating diarrhea and constipation. Preceding and during the diarrhea there is pain of a dull, griping, occasionally poignant nature which is located over the descending and sigmoid colon. The disease first attacks the rectum and lower sigmoid, so there is difficulty in expulsion of feces and there is associated tenesmus.

Frequent remissions(4, 96) and exacerbations occur and these follow some upper respiratory infection usually. There may be such prodromal symptoms as exhaustion, fatigue, slight spasmodic griping pain in the abdomen, and occasional sores in the mouth.

As the disease progresses the patient becomes anemic(96) with a general cachetic appearance, and the skin takes on a grayish-yellow tinge. The weight loss is

sometimes colossal. During the attacks the patient has a low, septic like type of fever, and a mild leukocytosis with polymorphonuclear cells predominating.

Such a clinical history arouses the suspicion of a chronic ulcerative colitis, but the actual diagnosis depends upon 1. stool examination, 2 digital rectal examination, 3. proctoscopy, and 4. roentgenology.

The stools(4, 61, 71) in advanced cases are semi-liquid to liquid, composed predominately of a pussy material much like the purulent expectoration of pneumonia. Blood is present in streaks or mixed throughout the stool and there is some mucus. Microscopically, there are mainly polymorphonuclear leukocytes along with some large phagocytic macrophage cells, and bacteria of chiefly the streptococcus variety. No parasities or ameba are found.

On digital rectal examination(4) the anus is seen to be spastic. The rectum is narrowed and tender and lacks the usual resiliency. If polyposis or granulation of the mucosa has occurred, there is a sensation of small polypoid protursions.

Proctoscopy and sigmoidoscopy are the most important diagnostic procedures. since the disease process begins in the rectal region, ninety five percent(20, 61) of the diagnoses can be made by proctoscopy, and in 20% of the cases(13)(111) , the lesions are so low that X ray

is of no use so that proctoscopy is the only diagnostic procedure in these cases. The pathognomonic picture(4, 43, 61) is a diffusely inflamed, granular, edematous mucosa that bleeds easily upon manipulation. However, the amount of ulceration and granulation varies with the pathological stage of the process.

The pathology(4, 13, 20, 96) is divided by Bui of the Mayo Clinic into four stages, 1. hyperemia and edema, 2. miliary abscesses, 3. miliary ulcers growing to larger ulcers, and 4. scarring and fibrosis.

The disease begins in the rectum(4, 20). The mucosa becomes hyperemic, and this is shortly followed by diffuse edema. In those cases where it is confined to the rectum it is seen that the diffuse inflammation gradually subsides and is replaced by normal mucous membrane as one progresses upwards into the sigmoid. The mucosa is thickened from the edema and the least amount of trauma causes it to bleed. Small ecchymoses may be seen scattered through the mucosa. At this early stage the part of the colon and rectum that is involved is spastic and contracted.

As the disease progresses small yellowish spots appear in the mucosa(20, 96). These are scattered diffusely throughout the bowel and on microscopic examination the capillaries are seen to be packed with erythrocytes.

Frequently, in the region of the abscess a terminal vessel is seen to be occluded with a thrombus.

These small abscesses(20) finally rupture through to the surface producing miliary ulcers which are follicular in nature. With secondary infection these ulcers gradually enlarge, become confluent, and may become serpigenous in outline(43). They are superficial mucosal ulcers, not as deep as those of amebic dysentery, and not as superficial as those of bacillary dysentery(88). Thus, in this stage(111) the colon presents a moth-eaten appearance and there is a granular, diffusely inflamed, ecchymotic mucosa that bleeds easily upon manipulation. The colon and rectum are now even more contracted than previously which imparts a tube like appearance.

Finally, after remissions(4, 20) the colon becomes fibrotic and scarred, and even more contracted. Sites of previous ulcers are replaced by pock like scars and as the mucosa regenerates over such areas small tabs, which frequently enlarge to produce a polyposis, project into the lumen. From fibrotic hyperplasia stenosis(77) of the rectum or sigmoid may also complicate the picture.

Roentgenology with a barium enema(Figure 4) is the second most important diagnostic procedure. Weber(114) describes the diffuse, symmetrical involvement of the circumference of the bowel and a creeping dogged type

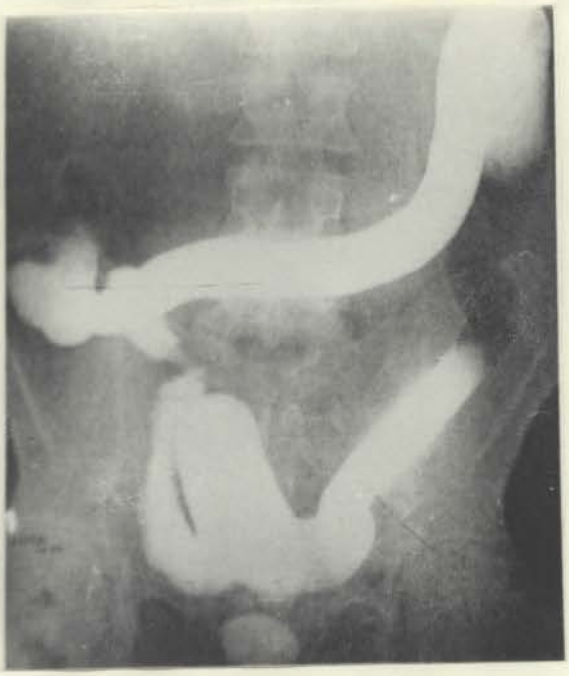


Plate 4: (a) Narrowing, shortening, mucosal destruction, and absence of haustral markings arecharacteristic of all ulcerative colonic disease; that the disease is most intense and progressed from the rectum is characteristic of chronic ulcerative colitis. (114, 115)
(b) Acute fulminating stage showing hazy, niche like mucosal border. (Not used)

of advance from segment to segment as characteristic. All colitis present similar general findings in the colon(Weber, 115), namely, evidence of mucosal destruction, and general contraction of the affected portion which includes narrowing, shortening, and mural thickening. The differentiation of the various types is based upon the site of apparent earliest and most severe involvement, the

distribution of the disease in the bowel, the direction of its extension, the intensity of the process, and the related X ray findings in other organs. Thus, in chronic ulcerative colitis, the rectum is first involved and the disease gradually progresses up the bowel, attacking its entire circumference producing concentric, uninterrupted, narrowing and shortening. The contours are smooth and straight, the haustral markings are lost, and there are signs of mucosal destruction depending upon the amount of ulceration at the time of the X ray. With a large amount of ulceration the mucosal border appears hazy, irregular, moth eaten, and fringed, but with fibrotic scarring the mucosal surface becomes smoother and more definitely outlined. Fluroscopy reveals rapid peristolysis and evacuation.

AMEBIASIS

Infestation with the endameba histolyticus causes a clinical history much like that of chronic ulcerative colitis. Usually it is slow in onset(43) with an incubation period varying from 1 to 13 weeks, and there is less prostration. Here the diagnosis is made by stool and tissue examinations for the ameba, proctoscopy, and roentgenology.

In amebic dysentery the stool and tissue examinations are the most important in establishing the diagnosis , and demonstration of the endameba histolyticus is pathognomonic. The bowel movements(96) are more frequent during the day than at night and consist(4,88) of a very loose, watery mixture of mucus andfresh blood, with a very little pus as contrasted to chronic ulcerative colitis. Microscopically the stools contain few leukocytes but many mononuclears. To obtain the best results, Brown and Magath(25) recommend that the stool for examination be obtained following magnesium sulphate catharsis. Then if the stool is examined immediately on a warm stage, they believe that one examination will reveal the ameba in 50% of the cases, a second examination will disclose it in 95% of the cases, and a third examination will diagnose nearly all of the affected patients. Specimens following oil catharsis are unsatisfactory(35) and likewise, those containing bismuth and arsenic crystals are not reliable. Therefore, two weeks(35) must elapse following a barium enema, and one week following medicines containing arsenic of bismuth.

The methods(25,35) of demonstrating the amebae are direct smear examination of the stools, study of stained smears, culture, and identification of the amebae in stained tissue sections.

Diagnosis by direct smear(35) is one of the most reliable available means of correct diagnosis. However, the specimens examined must be fresh and if liquid should be examined within 30 minutes. They should be kept warm in a temperature range of 37-40 degrees centigrade. The differentiation of the forms of ameba in the stools should be done by one well trained in their differential characteristics. The cysts(35)are generally found in formed stools, while the trophozoites are more numerous in loose stools. The cysts are best identified by staining the material with Lugols solution. DeYoung(35) states that when trophozoites are found containing numerous ingested red blood cells, the diagnosis is definite, and, when the trophozoites are found with the usual characteristics, although without ingested red blood cells, the diagnosis is probable..

DeYoung(35) believes that stained smears are the next most reliable method. The smears are stained with iron hematoxylin after fixation with Schaudinn's solution, and examined for the cysts and trophozoites. Cultures are less reliable since culturing often causes the endameba histolyticus and endomeba coli to become similar in appearance, and therefore, indistinguishable. Likewise, smears of the cultures are not reliable since nuclear changes occur making them indistinguishable.

Identification of the ameba in the tissues when applicable is also a good diagnostic procedure(25).

Until recently complement fixation tests have been tedious, difficult procedures, but recently Weiss and Arnold(116) report an improved procedure which in their hands has been very reliable.

The proctoscopic picture is characteristic, but is of use in only about half of the cases(96) since in this disease the pathological process begins in the cecum, and, although it extends distally, there are frequently no lesions in the rectum or sigmoid. When lesions are visible, discrete ulcers with undermined edges, and umbilicated floors are suggestive. These may be covered with a small amount of yellowish necrotic mucoid slough and surrounded by a circumscribed reddish halo. The ulcers are more widely disseminated, and deeper with a more punched out appearance, than those of chronic ulcerative colitis and between them, the mucosa appears either only slightly inflamed or entirely normal(4).

Roentgenology(Plate 5) offers less findings in this type than other types of colitis. There is a patchy irregular deformity of the colon with relatively uneffected loops in between(114) and the findings are those of narrowing, shortening, and thickening of the mucosa with evidence of some mucosal destruction. The haustral markings are

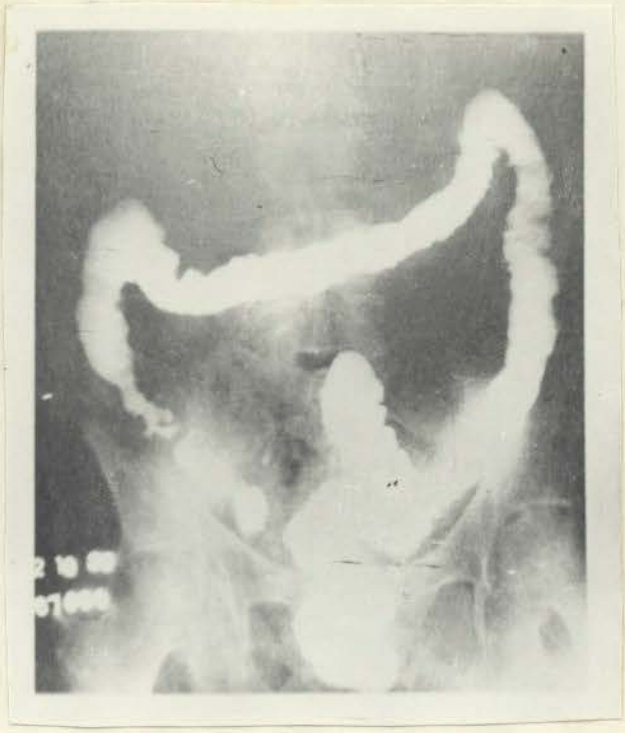


Plate 5: Chronic amebic ulcerative colitis. Narrowing and shortening are confined to the cecum, and the terminal portion of the ileum gives no evidence of organic change. (114/115)

more or less ironed out, but as a whole the irregular interrupted findings are not as intense as those in either chronic ulcerative colitis or tuberculous ileocolitis. The most severe involvement(115) is in the cecum and ascending colon, but the ileum is not invaded. However, a reflux of barium into the ileum from only partial distention of the cecum should always arouse the suspicion

of cecal disease. Frequently the X ray findings are so meager that they are only at best suggestive.

TUBERCULOUS COLITIS

In adults(88) intestinal tuberculosis is not known to occur excepting in connection with active tuberculosis elsewhere in the body, which is usually in the lungs. Felsen(43) states that in 85% there will be associated lung findings, and that rarely does primary tuberculosis of the intestine occur except in children.

The symptoms are those of tuberculosis combined with colon dysfunction(47). There is loss of appetite, loss of weight, tiredness, and flatulence. There is frequently pain or tenderness in the right lower quadrant associated with heavy meals. The diarrhea(88) is of gradual developement and is associated with alternating obstinate constipation.

The stools are rarely bloody(4, 61), but there is a persistent positive occult blood. Instead of the purulent discharge of chronic ulcerative colitis, there is a thin, watery, fecal stool containing undigested food. Microscopically, the tuberculous bacillus may be demonstrated (88, 43), but its presence is not too valuable since it may be found in the stools in pulmonary tuberculosis from

swallowing the sputum. A negative mantoux, however, is very significant in ruling out the disease.

Proctoscopic examination(4, 88) rarely aids in diagnosis since the lesions seldom extend to the sigmoid. However, when they do, they appear as deep ulcers with undermined and over hanging edges with normal mucous membrane in between. They are widely separated and difficult to distinguish from amebic ulcers. They tend to enlarge by circular extention around the cirumfercne of the bowel.

Photograph Was No Good

Plate 6: Tuberculous ulcerative ileocolitis. Narrowing, shortening, and loss of haustral markings, starting in the ileum where it is most intense and progressing caudad is characteristic.

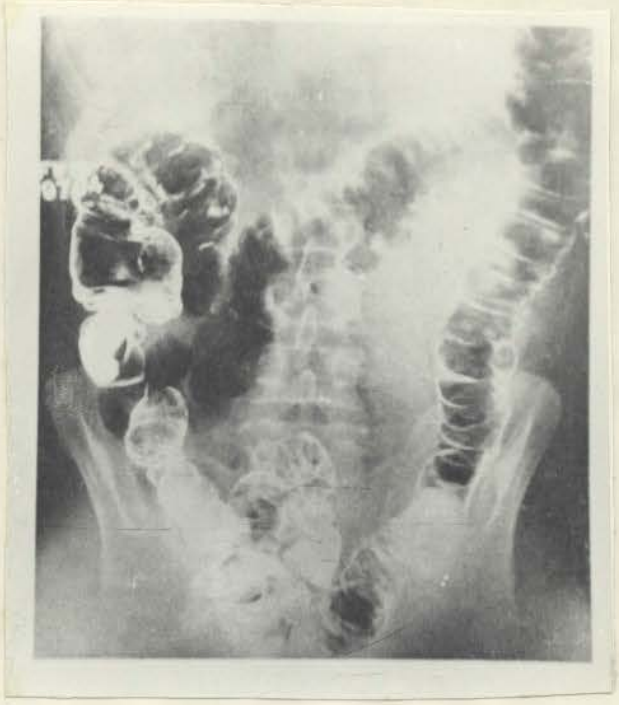


Plate 7: Hyperplastic tuberculous ileocolitis as revealed by the double contrast method. Abrupt narrowing of the terminal portion of the ileum, and deformity of the cecum are evident. (114, 115)

X ray is a very important aid in the diagnosis of intestinal tuberculosis. Flouroscopy shows spasticity and rapid emptying of the terminal ileum, cecum, and ascending colon(115, 88). The roentgenogram with a barium enema reveals that the process involves chiefly the terminal ileum, the cecum, and the ascending colon. In the ascending colon the findings become irregular, interrupted, and

patchy, and in the more distal portions of the intestine, there is less and less involvement. As in other cases of colitis there is narrowing, shortening, and thickening of the intestine with flattening of the haustrations. The mucosal border in the cecum and ileum is slightly hazy and ragged. In some cases there may be a funnel shapped narrowing or constriction. These findings are not as intense as in chronic ulcerative colitis, although they are more intense than in amebiasis.

The difference of tuberculous colitis and chronic ulcerative colitis may be summarized as follows:

	T. B. colitis,	C. U. C.
Loss of wt.	gradual	rapid
Lungs	pulmonary T. B.	clear
Location	ileum & cecum	rectum and sigmoid
Stools:		
Blood	slight	profuse
Organism	tuberculous bacillus	numerous types of organisms and especially strept.
X ray	findings less intense, and progress down the colon	findings very intense, and progress up the colon.
Sigmoidoscopy	rarely lesions	diffuse involvement and ulcerations
Symptoms	gradually progressive alternating diarrhea & constipation.	remitting severe diarrhea.

BACILLARY DYSENTERY

Bacillary dysentery(4, 43, 61, 88) is a more acute colon disease characterized by an acute onset following

a short incubation(43) and consisting of violent abdominal cramps(88), rise in temperature to a fever as high as 103-4 degrees, general malaise, and diarrhea. At the onset the pain is generally severe, and there is evidence of marked toxemia.

The diagnosis is made by demonstrating the bacilli in culture from the stools and by blood agglutination.

The stools(88) are composed of mucus, and blood, but contain much smaller amounts of pus than in chronic ulcerative colitis. Positive cultures for the Shiga, Flexner, and Sonne bacilli may be obtained in the first four days(61) and less frequently up to the tenth day.

Blood agglutination of the bacilli can be obtained from the 10th day on(61), and Felsen(42 believes a 1:100 or greater agglutination diagnostic of Flexner and Shiga types and a 1:150 or greater agglutination diagnostic of Sonne types. However, to complicate things Paulson(90) found in his work that occasionally negative agglutination reactions occur when the specific organisms have been know to occur in the stools, and Penner(93) describes temporary non-agglutination in known cases of bacillary dysentery.

The sigmoioscopic picture(88) is very similar to that of chronic ulcerative colitis with a rather diffuse

involvement of the rectum and sigmoid, but the ulcers of bacillary dysentery are more superficial involving only the superficial layers of the mucosa.

Roentgenology(88, 115) is of little value since in the acute stages a barium enema is seldom advisable.

However, this acute phase of the disease may not subside in a short time as it usually does, and then it goes into a chronic stage(88) that closely resembles chronic ulcerative colitis. The differentiation in these cases depends upon the history of the acute period of the disease and the agglutination properties of the blood. The finding of a bacteriophage in the stools specific for the dysentery bacilli also is of some significance in the diagnosis of these cases(42,44).

TYPHOID FEVER

Typhoid fever is an acute disease that practically never recurs so it need not be considered here.

II. Non-ulcerative organic disease

This group of the intestinal diseases causing diarrhea is more easily differentiated and, therefore, need not be considered so completely.

POLYPOSIS

Polyposis(4) of the colon may be of three different types 1. Polyposis secondary to chronic ulcerative colitis, 2. congenital polyps, and 3. adenomatous polyps. The secondary and congenital types may be scattered diffusely throughout the bowel, while the adenomatous polyps are either single or few in number.

The symptoms(96) of polyposis consist of abdominal pain, diarrhea of bloody, mucus stools, and occasionally nausea and vomiting. The abdominal pain is of an intermittent cramp like nature, and the diarrhea appears periodically. In the secondary type the polyposis occurs after a considerable duration of the colitis, and in the congenital type the symptoms usually appear in the early part of the third decade. Thus, both may appear in the same period of life. The adenomatous polyps, however, occur chiefly in senescence.

The diagnosis(4) is made by sigmoidoscopy and roentgenology. Sigmoidoscopy reveals multiple small polyps which are scattered diffusely throughout the bowel. The polyps secondary to colitis are superimposed on a granular, scarred, membrane, while those of the congenital type protrude from a more normal mucosa.

X ray(115) by the double contrast technique originally described by Fischer reveals these quite well. (Plate 8:). This technique consists first of a barium

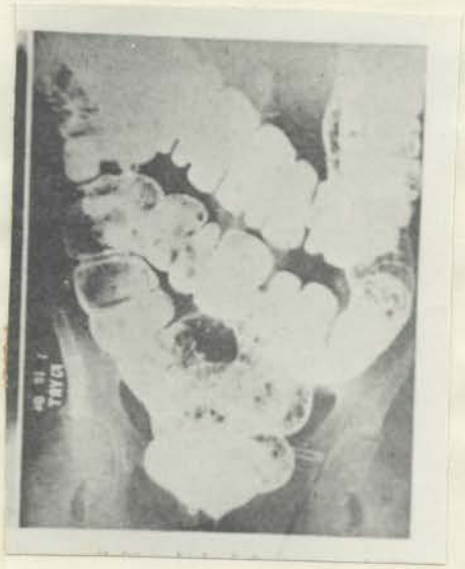


Plate 8: Diffuse polyposis as revealed by the double contrast technique. The lacy appearance is pathognomonic.(11)(15)

enema with the usual distention of the colon, second evacuation of most of the barium, and lastly redistention of the colon by air or inert gas. By such procedure the opaque material settles into the crevices of the villous adenomatous tissue, giving a pathognomonic lacy internal relief pattern.

Digital rectal examination(4) helps differentiate the secondary and the congenital types of polyps in that the rectal lumen is narrowed, the wall is resistant, and

there is a lack of the normal resiliency in polyposis secondary to chronic ulcerative colitis, but the rectal lumen is of normal size, and the mucosa is soft, velvety, and pliable in congenital polyposis.

DIVERTICULOSIS AND DIVERTICULITIS

Diverticulitis(4, 88) gives a history of irregular distress along the colon with a sudden superimposed syndrome similar to that of acute appendicitis. There is generally a history of constipation, but there may be a diarrhea.

Roentgenology following a barium enema is diagnostic (4, 88) after the acute stage has subsided and shows outpocketings along the colon filled with the barium.

NEOPLASTIC AND GRANULOMATOUS DISEASE

There is a history of bowel irregularity of a gradually increasing severity and X ray findings are characteristic.

III. Parasitic infestations.

The manifestations(71) of parasitic disease in the colon are variable and are diagnosed by the finding of the various cyst and trophozoite forms in the stools upon microscopic examination. The types that may be encountered include coccidiosis; giardiasis caused by the flagellate

giardia lamblia; flagellate diarrhea caused in this country by trichomonas hominis and chilomastix mesnili; malarial dysentery caused by the blocking of the smaller blood vessels by the sporulating subtertian parasities which inturn produces the hemorrhages; leishmanial dysentery which is very rare and caused by leishman-donovan bodies; and lastly balantidium coli infestation which produces an associated severe clinical anemia.

IV. Diarrhea due to systemic disease.

Both the mucous colitis(71) and the nervous diarrheas (5) are associated with a nervous type of individual and blood is rarely presnet. Sigmoidoscopy(71) in mucous colitis reveals a pale, rather yellow appearing, membrane coated with ropes of viscid mucus. The mucosa appears dry and unhealthy, but no ulcerations are present.

Any allergy diarrhea is generally associated with other hypersensitivity phenomenon such as migraine, hay fever, asthma, eczema, urticaria, and food idiosyncrasies. A familial history of allergy can be elicited in most cases and in studying the patients, elimination diets will reveal food sensitization. Bacterial sensitization also may be discovered. In these cases the diarrhea is more apt to come on very suddenly and seldom contains blood (48, 50).

SPRUE

The classical picture of sprue(73) consists of a voluminous steatorrhea, oral and tongue lesions with the loss of lingual papillae and marked redness of the mucosa, low stomach acidity or complete achlorhydria, and a hyperchromic macrocytic anemia.

The cause of the disease is not known so it may therefore be better described as a syndrome. Recently the opinion that it is a deficiency disease has been gaining influence(49).

There are few pathological findings. There may be a fibrosis of the pancreas and there usually is an atrophic enteritis(49). There frequently may be no demonstrable changes at all in the intestine(97), but usually there is chronic inflammation and edema of the intestine along with atrophy and atonia of the intestinal wall. Serum calcium and serum phosphorus are low and many authors believe a low blood sugar one of the most helpful differential findings in the diagnosis of sprue(49).

Subjectively, there is a voluminous steatorrhea consisting of large, pale colored, bloodless, pungent stools containing as much as 25-50% fat(49, 97). There is either a low or a complete achlorhydria of the stomach, and there is evidence of osteoporosis. A macrocytic hyperchromic anemia is quite constant.

Associated with this syndrome is a rather characteristic although not pathognomonic X ray picture of the small intestine. There is variation in the size of the intestinal loops occuring most frequently in the ileum, less often in the jejunum, and rarely in the duodenum. In severe sprue the intestinal loops often appear atonic and may dilate to nearly the size of the large bowel, while in intermittent areas there may be spasticity. There is distortion of the mucosal pattern, also chiefly confined to the jejunum, and the ileum. The normal delicate feathery pattern of the jejunum is replaced by a much coarser appearance simulating the appearance of the colon. Lastly, the barium is distributed through the bowel in a segmental arrangement presenting a sausage like appearance which is seen usually in the middle and lower ileum and is attributed to areas of spasticity and dilitation. Occasionally the terminal ileum is straight and rigid. The colon, however, is essentially normal in appearance.

PELLAGRA

Pellagra consists of a syndrome much like that of sprue, but in addition there is added a dermatitis, and a dementia, which composes the classical triad of diarrhea, dermatitis, and dementia(96).

The dermatitis is distributed over the wrists and forearms and occasionally around the neck, and is typically confined to these areas. The lesions vary from blotchy erythema in the acute phase to a dry, scaly lesion later on in the process.

The diarrhea is frequently intractable and consists of loose, watery, stools containing undigested food, but there is no blood.

DIAGNOSIS OF THE FAMILY

Mr. Klinge, Mr. Tilse, Mrs. Tilse, Willie, and Anna Tilse have never been to a doctor to have a systematic examination so that in them the diagnosis depends entirely upon the clinical history. Although a diagnosis of chronic ulcerative colitis without roentgenograms, and proctoscopy is not very dogmatic, the clinical syndrome in each of these cases is very characteristic. Mr. Klinge, Mr. Tilse, and Willie Tilse had a long chronic history of recurrent diarrhea which was composed chiefly of pus, and blood, and this is the classical story of chronic ulcerative colitis. Anna Tilse and Mrs. Tilse had only a mild involvement, but it also is suggestive of chronic ulcerative colitis. Since the endameba histolyticus was not found in any of the four children who had lived

with these afflicted relation for years, it is not at all probable that they suffered from amebic dysentery. It is true that an atypical endameba histolyticus was found in one of the children, A. W. Tilse, but it was found only twice out of numerous examinations, and a second laboratory failed to confirm it. Thus, there is some question as to whether it really was the endameba histolyticus or not, and, if it was, the patient had been away from home for seven years before acquiring intestinal symptoms. There is, furthermore, no history of tuberculosis, and no history of an acute onset of their diarrhea as might be expected with bacillary dysentery. Dysentery bacilli were not found in any of the five children that were examined, but unfortunately blood agglutinations for the Shiga, Flexner, and Sonne types of the dysentery bacilli were not performed. Thus, chronic ulcerative colitis seems the most probable diagnosis.

Marie and Arnold Tilse had very characteristic symptoms and findings of chronic ulcerative colitis and were thus diagnosed by the Mayo Clinic.

A. W. Tilse had a characteristic proctoscopic picture and clinical syndrome of chronic ulcerative colitis, but the X ray was essentially normal. He had a polyposis which was suggestive of the secondary type which follows chronic ulcerative colitis, but he had apparently not

had the disease long enough for polyp developement. Out of 558 complications(10) which represented 15% of the cases of chronic ulcerative colitis seen at the Mayo Clinic, 130 of them were polyposis. Therefore, we see that they quite commonly follow ulcerative colitis. No other member of the family had polyposis, which would be against familial polyposis, and the large polyp in the rectum from which a biopsy was taken revealed the tissue to be of an inflammatory nature. Thus, it is most likely that the polyps were due to the inflammation. An atypical endameba histolyticus was found in the stools two times out of several examinations, but was not verified by a second laboratory. Iron hematoxylin stains of tissue from the rectum contained no amebae, and the patient did not respond to amebic treatment, so it is likely that he did not have colitis from an ameba infestation. Therefore, the best conclusion is that he suffered from chronic ulcerative colitis of a rather atypical nature.

L. H. Tilse had a different syndrome than the other members of the family, for his symptoms were all related to an obstructive syndrome. Operation confirmed the diagnosis of a non-specific terminal ileitis. Felsen(42) believes that distal ileitis and chronic ulcerative colitis are different manifestation of the same disease, and Cattell(31) noticed that the terminal ileum is involved

in 20% of the acute cases of chronic ulcerative colitis. This is interesting since the earlier symptoms of this patient's trouble were suggestive of a colitis, but as he progressed they changed into those of a terminal ileitis. This gives rise to the question of whether or not the patient did have colitis to begin with which later changed into an involvement of the ileum while the colon recovered. The patient's colon was not examined earlier in the disease so this is only an hypothesis.

Leonard Tilse has a clinical history suggestive of ulcerative colitis and, when at the Mayo Clinic, he did have some colon findings suggestive of it. The diplostreptococcus of Bargen was found in his stools and, since this has been found in only 3-4% of patients that did not have a chronic ulcerative colitis at the Mayo Clinic(28), this is also suggestive of the disease.

However, as he progressed, the picture changed and autopsy revealed that he suffered from an enteritis of characteristics similar to those of the non-specific ileitis except that most of the small intestine was involved. The final stage resembled sprue, but seldom is there found much pathology in the intestine other than atrophy. Cases of deficiency disease frequently develop in inflammations of the intestine(16, 39, 58, 102) so it is likely that he died of a fulminating non-specific

enteritis which was complicated by the deficiency disease sprue. Earlier in the disease he had had the findings of a mild ulcerative colitis, and there is the possibility that the enteritis was a different manifestation of the same type of process. Such conclusions are merely supposition, however, and are not supported by present experimental findings, but further investigation along this line would be interesting.

ETIOLOGY

There have been many theories offered in regard to the etiology of chronic ulcerative colitis. Its origin has been thought to be due to:

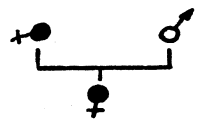
1. A familial or hereditary weakness with secondary infection,
2. A bacterial infection,
3. A filterable virus,
4. Dietary deficiency,
5. Allergy or sensitization to foods or bacterial products, and, lastly,
6. A metabolic derangement with lowered resistance.

HEREDITARY OR FAMILIAL PREDISPOSITION

Very seldom does chronic ulcerative colitis occur in more than one member of the same family and thus there has been very little attention directed towards the possibility of a familial or an inhereted predisposition to ulcerative colitis. In over 1600 cases at the Mayo Clinic since 1924, Bargen(6) has found only 18 cases in which more than one member of a family had the disease. Other men have noticed a similar scarcity.

However, Moltke(75, 76) has recently directed attention toward the possibility of a family factor and has presented five families with multiple cases. Two of the families had a severe type of the disease and the other three had more of a mild form.

Family No. 1

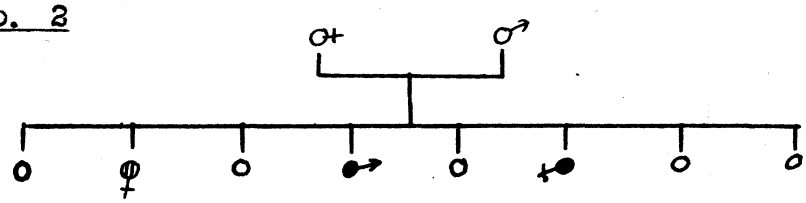


●--afflicted
○--non-afflicted

The mother died in 1909 after a typical history of a remitting diarrhea of pus, blood, and mucus, and autopsy at the Aalborg clinic revealed that she had had ulcerative colitis.

The daughter died in 1932 at the age of 36 after a five to six year history of blood in the stools. She alternated with obstinate constipation and diarrhea, and two months before she entered the Municipal Hospital of Copenhagen, she began to have 5-6 stools per day consisting of a bloody, pussy diarrhea along with much tenesmus. At entrance her hemaglobin was 60%. Twenty cenimeters of the lower bowel were seen to be red and hemorrhagic with small hemorrhagic dots, by proctoscopic, and the entrance of the proctoscope caused some bleeding. She gradually became worse in the hospital and in spite of transfusions died. Autopsy confirmed the diagnosis of chronic ulcerative colitis. She was not affected until 17 years following the death of her mother.

Family No. 2



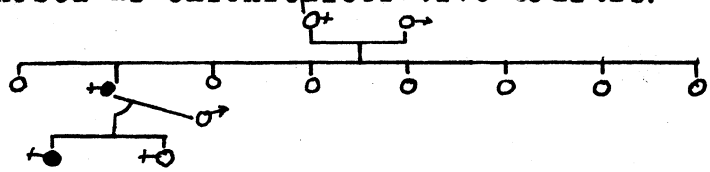
In this large family of brothers and sisters two died of chronic ulcerative colitis, and a sister was slightly involved. One brother died at the age of 33 in 1931. He had had symptoms for a duration of five years consisting of an occasional slight bowel bleeding which he thought was due to hemorrhoids. However, following hemorrhoidectomy he developed a violent diarrhea, with rising fever, and died. Proctoscopic at the onset of the diarrhea revealed a firey red mucous membrane with diffuse swelling and edema and there were a few small erosions. X ray showed a lead pipe colon. Necropsy confirmed the diagnosis of ulcerative colitis.

Three years after his death a younger brother developed a similar bleeding which he thought due to hemorrhoids. After 1½ years duration he too developed a severe diarrhea and in spite of repeated transfusions died at the age of 27 in 1934. Necropsy again confirmed the diagnosis of chronic ulcerative colitis. In neither case were there any pathogenic bacteria found.

A sister had for some time slight bleedings from the bowels. X ray showed some narrowing of the sigmoid, but nothing else. Later when seen at the hospital proctoscopy showed no disturbance.

Family No. 3

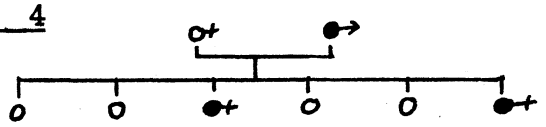
In the remainder of the families the course was not so fulminating and none of the members died, but they were diagnosed as chronic ulcerative colitis.



The mother at the age of 42 in 1936 began to suffer from abdominal pain and bloody discharges from the anus. This continued remittently until 1938 when she was seen at the Municipal Hospital of Copenhagen. Proctoscopic revealed a readily bleeding mucosa with edematous swelling and this was covered by a purulent secretion. Her stools were thin and slimy containing blood. She improved with 0.5% gallotannic acid enemas. In 1934 she was again readmitted because of a duodenal ulcer. At that time she had no symptoms from her ulcerative colitis, but proctoscopic revealed a pale, succulent readily bleeding mucosa. Her daughter became ill at the age of 23 in 1932, and, after one years duration, was admitted to the hospital complaining of a diarrhea of blood, and mucus with 6-8 stools per day. Proctoscopic revealed a dark red succulent mucosa covered by a greenish-gray purulent discharge. She gradually improved with gallotannic acid enemas, but suffered recurrences. However, she is still living. The mother and daughter were never together when they had

the disease so that there was no way that they could have obtained it through infectious contact.

Family No. 4

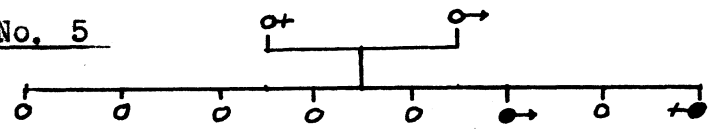


The father appeared at the hospital at the age of 55 in 1930 after having a recurrent diarrhea for a period of 15 years. His sigmoid mucosa was seen to be profoundly inflamed, and almost villous in nature with a profuse secretion of pus and blood. Later he died of cardiac trouble, but an autopsy was not obtained.

A daughter came under care in 1929 at the age of 24. She complained of blood in her stools with slight abdominal pain, and constipation rather than diarrhea. However, proctoscopy revealed a typical proctosigmoiditis with a fiery red slightly bleeding membrane. X ray revealed no polyposis, and, thus, the possibility of a hereditary polyposis as suggested by the villous nature of the father's colon is ruled out. No pathogenic bacteria were found in either of their stools. The daughter was in contact with her father, however, and here contagion cannot be ruled out.

Another daughter away from home developed bleeding from her bowels during pregnancy, but when examined was well.

Family No. 5



The brother was seen at the Rigs hospital at the age of 24 in 1930 after a three years duration of alternating constipation and diarrhea consisting of bloody, mucous stools. Proctoscopic showed a typical appearance of a chronic ulcerative colitis. He was not well for some years afterwards but was greatly improved by yatren therapy.

The sister was seen at the Aarhus Municipal Hospital at the age of 23 in 1933. She had had intestinal bleeding of a recurrent 14 years duration. Again proctoscopic revealed a chronic ulcerative colitis. She responded poorly to treatment and has not been entirely well since. These two were widely separated so that there could have been no contagion.

Thus, we see that there was no possibility of contagion in most of these, and no pathogenic bacteria of the usual dysentery or salmonella groups in the stools. Polyposis was found in none.

These families were encountered in a series of 117 patients and were personally examined or talked to by Dr. Moltke. It was not possible to trace all of the members of all of the families so that there may have been

more. In ad ition four other families gave a history as follows:

1. One man said that his sister had the same malady only to a more severe degree and more constantly.

2. A woman said her mother had suffered from diarrhea of a bloody, mucus, foul smelling nature.

3. A women stated that her maternal grandfather had bled from the bowels, and lastly,

4. A man said his father suffered from repeated bleeding from the bowels.

Moltke states that Mummery apparently saw one family that contained two members with the disease and another family in which a sister of one of his ulcerative colitis patients had apparently died with intestinal hemorrhage. Spriggs reported a family with 3 members who had ulcerative colitis without having anything in common that might explain it by infection by contact.

Therefore, Moltke wishes to place himself among those who have their doubts as to the role infection plays in the cause of chronic ulcerative colitis, and, although the etiology and pathogenesis of chronic ulcerative colitis, is unknown, he suggests the possibility of a genetic factor in the individual which acting alone or with another factor produces the disease.

RELATIONSHIP TO THE TILSE FAMILY

The Tilse Family have a familial history of nine members out of twelve that had an intestinal disease associated with diarrhea. Two of them, Marie and Arnold, had a definite chronic ulcerative colitis; four of them, Mr. and Mrs. Tilse, Willie, and Anna have a clinical history typical of chronic ulcerative colitis; two of them Leonard, and W. W. Tilse, had a mild chronic ulcerative colitis; and one, L. H. Tilse, had a terminal ileitis. There could have been no possibility of contagion in four of them, A. W. Tilse, L. H. Tilse, Leonard, and Anna, and, although the remainder have been exposed to the disease from another member of the family, they did not themselves acquire the disease for several years after the first contact. Furthermore, no one else in the community ever obtained the disease. Thus, contagion can be pretty well ruled out. Therefore, this familial history is very suggestive of some genetic factor that produces or acts as a predisposing factor in the production of the disease in this particular family.

BACTERIAL INFECTION THEORY

For years many investigators have believed that chronic ulcerative colitis is due to some infection.

Complications such as arthritis, and systemic abscess(10), and symptoms such as fever and leukocytosis suggest that it is of an infectious nature.

Since 1924, Bargen of the Mayo Clinic has been investigating a gram positive diplostreptococcus as the etiology of chronic ulcerative colitis(6, 12, 13, 28), and he has performed more conclusive experimentation than any other man. The organism(13) is a gram positive lancet shaped diplostreptococcus that occurs in pairs and occasionally in groups of four. It does not ferment inulin, or mannite, but does dextrose, lactose, saccharose, maltose, raffinose, salicin, and acidified milk when tested immediately. It differes from the enterococcus both in fermentation reactions and in heat resistance as a temperature of 60 degrees centigrade kills Bargens organism, but the enterococcus survives(95).

This diplostreptococcus(6) has been isolated from the stools in 80% of the group of 1600 or more patients that have been seen with chronic ulcerative colitis at the Mayo Clinic. It has been obtained from periapical dental abscesses(28), and has occasionally been cultured from the blood in severe cases of the disease. In a series of 100 normal controls(28) the diplostreptococcus has been found in only four cases.

Injection of the different strains isolated from the ulcerations of human colitis intravenously in rabbits has resulted in the production of lesions resembling those seen in the colon of man in 65%(38). Similarly injections of cultures into dogs produced in 21 out of 25 cases a typical severe diarrhea of characteristic bloody nature, and on examination they found lesions in their colon similar to those in ulcerative colitis patients (96). The diplostreptococcus isolated from periapical dental abscesses from 148 patients(38) produced typical lesions in 75% of the animals. However, cultures from the nose and throat of 534 patients produced lesions in only 0.8% of experiemental animals. Furthermore, in those cases where lesions were reproduced in animals the diplostreptococcus could again be obtained from those lesions by culturing.

A special culture technique(13, 96) is used. Swabs from the lesions of a patient are cultured in dextrose brain broth and then transferred to blood agar and lactose agar plates. After incubation for 24 hours on blood agar the colonies are surrounded by a green zone with a faintly hemolytic zone between it and the colony.

Furthermore, patients with chronic ulcerative colitis that have had remissions have been shown at the Mayo Clinic

to have agglutination titres with the diplostreptococcus as high as 1:10,000 and generally above 1:1,000(96). This data along with the excellent theraputic results with the diplostreptococcus serum has led Dr. Bargen and others at the Mayo clinic to believe that the diplostreptococcus is the etiological agent of chronic ulcerative colitis.

Thorlakson(109) and others such as Yeomans(120), Brown(26), Einhorn(38) have considered the dysentery bacillus responsible for the disease, but none of them have supported their views with extensive investigations. Felson(42, 44) has studied 400 cases of bacillary dysentery in relationship to chronic ulcerative colitis. In a series of 81 cases, there was only one that did not have a positive agglutination test. Three others were diagnosed as bacillary dysentery by demonstrating the organism in the stools. In every one of these cases where X ray was done, the findings were typical of chronic ulcerative colitis, and necropsy in two cases, and surgical pathology in another revealed a chronic ulcerative colitis. Therefore, it was inferred that these patients had had bacillary dysentery and had gone into the chronic stage or chronic ulcerative colitis stage of the disease.

Following the Jersey City epidemic of bacillary dysentery(44), 122 of the 210 patients were followed for nine to twelve months. Of this group 37.7% had

persistent or recurring intestinal symptoms or signs; eight or 6.5% had diarrhea with blood, mucus, and pus 12 or 9.8% had a watery diarrhea without gross blood, 3 or 2.4% had bloody evacuations without diarrhea, and 23 or 19% had miscellaneous intestinal disturbances such as recurring attacks of abdominal cramps. The eight with diarrhea of blood and pus gave typical findings of chronic ulcerative colitis; two others presented a characteristic proctoscopic appearance; and 3 other cases of chronic distal ileitis were found at surgery and at necropsy. Thus, 13 out of the 122 or 10.7% developed typical chronic ulcerative colitis. Felsen(44) and Paulson(90, 92) also point out that the pathology of bacillary dysentery and chronic ulcerative colitis is similar. There is diffuse inflammation covered with a purulent blood tinged exudate, and the ulceration later goes on to fibrosis in both. This, further, arouses the suspicion that chronic ulcerative colitis is at least in part a chronic stage of bacillary dysentery. Winkelstein and Herschberger(117) found dysentery organisms in 7 out of 60 typical cases of non-specific ulcerative colitis, the bacteriophage potent against one or more strains of dysentery organisms was present in the stools of 15 or 36% out of 41 cases of ulcerative colitis, and

there was a positive serum agglutination for dysentery organisms in 27 or 22% out of 120 ulcerative colitis patients. Furthermore, Paulson(90) has pointed out that in some cases patients have negative agglutination reactions when dysentery bacilli have been known to be cultured from their stools.

Bargen(96) on the other hand has studied a series of cases seen at the Mayo clinic according to the methods of Felsen, and Paulson including stool cultures, and agglutination, but has failed to find any relationship between bacillary dysentery and ulcerative colitis. Mackie(67) believes the bacillary dysentery may predispose the patient to chronic ulcerative colitis, but thinks it incredible in view of the virulence of the organism and the paucity of the organisms found in ulcerative colitis, that the dysentery bacilli could cause the disease.

Therefore, we must conclude that bacillary dysentery in a few cases is a definite predisposing factor, and that it may account for a few of the chronic diarrheas, but there is insufficient investigation and controled experimentation to prove that it is definitely the etiological factor for all cases.

Some investigators believe that chronic ulcerative colitis is simply undiagnosed amebic dysentery(99). Dr. Tollman(108) has found the amebae in stained

microscopic tissue sections when it was not found clinically. Thus, there may be an occasional case of amebiasis that may be mistaken as chronic ulcerative colitis, but, since the pathology is not like that of a classical ulcerative colitis, these cases are probably few.

Other theories of bacterial origin have been suggested from time to time, but none of them have been supported by investigation. Bassler(17) believes that the disease is due to a symbiotic relationship of several organisms, and he believes that the most important of these are the hemolytic streptococci, streptococci viridans, nonhemolytic streptococci, and some of the normal denizens of the colon namely, alcaligenes fecaloides, staphylococcus albus, clostridium welchi, and clostridium oedematis maligni, eberthella coli of specific types, enterococci, pseudomonas aeruginosa, and erythrobacillus prodigiosa. Blake and Higs(22) have incriminated B. proteus, B. pyocyaneus, B. lactis-aerogenes, and B mucosus capsulatus. Hemolytic B. coli(92) has been thought to be the cause, but Nicholls(86) can find no difference between it and the normal B. coli that is indigenous in the human bowel. Dack, Dragstedt, and Heinz(33) found bacterium necrophorum in the ulcers and stools of patients with chronic ulcerative colitis, but this bacterium is not found when the ulcerations heal. Thus, they believe that

it is significant in the etiology. However, none of these have been supported by experiemental investigation.

BACTERIAL ETIOLOGY IN THE TILSE FAMILY

The Bargen diplostreptococcus was found in only one of the five Tilses who were examined. The diplostreptococcus serum seemed to help them theraputically, but apparently the diplostreptococcus was not the cause of the disease.

None of the Tilses gave a history of an acute, brusque onset of their symptoms, and in most of the cases contagion could not account for the transmission of the disease from one member to another. Furthermore, there was never at any time anyone else in the community where they lived that suffered from a diarrhea disease, although several of their neighbors had eaten with the family on several occasions. Therefore, although agglutinations were not performed on them, it seems improbable, but not conclusive, that bacillary dysentery is the cause of their disease.

The endameba histolyticus was found in only one of the five examined and as has been explained it may have been questionable in him. Contagion did not occur and, thus, the disease is not likely due to amebiasis.

No other infectious bacteria were found. Therefore, apparently no specific bacterium can be named as the cause of the disease, but unquestionable streptococci and other bacteria were secondary invadors of the ulcerations.

FILTERABLE VIRUS

Mones and SanJuan(77) have investigated the possibility of a filterable virus as the etiologic agent. They took scrapings of ulcers of ulcerative colitis patients and made emulsions in sterile physiologic saline solution. These were filtered through a porcelain filter(L. 3) and the filtrate injected into the brains and veins of rabbits. The lesions thus produced in the rabbits were remarkable and sometimes were situated in the intestine, and no lesions were encountered in the controls.

The virus is isolated by scraping ulcers four or five times after first cleansing the bowel by a 1000cc normal saline enema, and these scrapings are placed in 20cc of sterile physiologic saline. The tube is then shaken and filtered through paper and lastly through a new, sterile, dry, porcelain filter (L 3) and the filtrate then kept in iceboxes at 1-5 degrees centigrade.

This virus could be administered subcutaneously, intravenously, or intracerebrally with the same result.

Three cc per kg. was used for rabbits, 1cc/kg for the guinea pigs, and only 0.5cc/kg. for the dogs. After administration the virus could be obtained from the animal from any part ofthe body and especially from maceration of the spleen. They considered it isolated only when it could produce the disease in a series of animals. Each successive passage through an animal decreased its potency until gone in the 4th or 5th passage. Fifty-five percent of the filtrates, and 88% of the filtrates passed through Rosenow's culture medium produced lesions when injected into the rabbits.

"In the digestive tract of the animals were found lesions which varied from simple congestion to deep ulceration; however, the most frequent lesions were small hemorrhages into the mucosa and submucosa. These lesions were particularly frequent in the rectum and small intestine. When animals lived more than one month, these lesions produced stenosis. Hemorrhagic and desquamative changes were occasionally seen in the stomach, liver, kidneys, suprarenal glands, and nervous system. About 50% of the rabbits that received injections of the virus died within ten days and 10% died between 20 and 50 days."

In dogs their experiemental results were more similar to the disease in man than it was in rabbits.

A few days after the injection, the dogs began to have a diarrhea of a large amount of bloody stools. Some continued to become cachectic until they died, while others seemed to overcome the disease only to suffer recurrences ten to twelve days later. Necropsy revealed that they had ulcers in their digestive tract extending from the stomach to the rectum.

Mones and SanJuan(77) believe the lesions to be initially formed in the blood vessels. They believe the virus causes emboli from its attack on the endothelium of the blood vessels, and thus blood passes out into the connective tissue. These perivascular hemorrhages compress the vessels causing obliteration and the intestinal villi become congested and edematous with desquamation of the epithelium and small hemorrhages. This then produces a good implantation for other bacteria especially the streptococcus which becomes a secondary invador.

This is interesting experimental data, but is not conclusive. However, it should be considered and studied further, for if confirmed and properly controlled, it may prove to be a very striking piece of work.

POSSIBILITY OF VIRUS IN THE TILSES

There is no evidence to support an opinion either for or against. Virus diseases are generally highly

contagious, but as shown before this disease was not contagious. Nevertheless, the disease may be due to a virus.

DIET DEFICIENCY

Davis(34) points out that a Vitamin B deficiency causes anorexia, anemia, degenerative changes in the intestinal tract such as the reduction in the size of the villi, decreased absorptive capacity, decreased muscular vigor, vascular and trophic changes in the mucosa, and degenerative changes in the nervous system. Furthermore, Vitamin G deficiency produces vague digestive upset, mental depression, skin lesions, stomatitis, pellagra, diarrhea, and also nervous system degeneration. Vitamin G deficiency causes an ischemic edematous colon mucosa that bleeds easily in animals. Therefore, he believes such a deficiency followed by a superimposed secondary infection a plausible explanation of the etiology of chronic ulcerative colitis. He, furthermore, points out that vitamin B is destroyed by heat, and, although vitamin G is heat stable, the solubility in water is decreased by boiling so that this may account for their deficiency in the average diet.

Barnes(16), Eusterman(39), Snell (102), and Jones(58) have described deficiency syndrome in ulcerative colitis.

Mackie (67) found 63% of 75 ulcerative colitis cases showing some deficiency phenomena such as lingual and buccal mucous membrane abnormalities, skin alteration, low blood constituents and the like.

However, Mackie(67, 68) believes that these defeciency phenomena are not the cause of the colitis, but in reality the ulcerative colitis is the cause of these defeciency findings since they are only associated with the latter stages of the disease. He, furthermore, points out that in deficiency disease there is a sluggish atonic bowel action as shown by the time for charcoal elimination after ingestion, rather than the spasticity which is encountered in colitis. Experimental work in animals is quite striking, but it seems improbable that any human would exist on such a rigidly restricted diet, regardless of economic status, so as to produce such a deficiency.

Bargen and Kemble(12) studied 20 consecutive patients with reference to dietary deficiency as a predisposing factor. However, in all of these cases the diets were adequate.

Therefore, it seems that dietary insufficiency is not significant as a predisposing factor in most cases and that the deficiency phenomena that develop are all secondary to the colitis.

RELATION OF DIET TO THE TILSES

The diet of the family while they were at home was always adequate. It included all kinds of meat in adequate quantities, cereals, vegetables of all kinds including potatoes, occasionally fruits, large quantities of milk, and in the summer time plenty of green vegetables. These foods were supplied in more than adequate quantities, and were cleanly, and carefully prepared. After the boys were away from home they occasionally didn't eat regularly or adequately as in the case of Arnold Tilse, but none of them had any deficiency symptoms until their disease had been present for some time. Therfore, what deficiency symptoms that did develop were apparently the result of their colitis and were not the cause of it.

ALLERGY

Mackie(67, 79) has found that marked, predictable variations in bowel symptoms occur following the inclusion or the exclusion of certain foods in the diet. In 65 patients 33 or 50.5% gave a definite clinical evidence of active food allergy. A variety of foods were found to be the cause of these sensitization reactions and in order they were milk, wheat, egg, spinach, and orange.

The addition or exclusion of these foods resulted in a prompt exacerbation and nearly as prompt a remission. In the acute phase the test diets gave no indication of food sensitization, but four months later in one case a mild recurrence of symptoms was promptly checked by resorting to diet consultation. Hare(50) and Andresen(1) point out that the proctoscopic picture may be quite typical of ulcerative colitis. The allergic response consists of increased permeability of the capillaries producing edema and there is spasm of unstriped muscle. Frequently this goes on to actual ulceration. Hare(50) noted that in 38 cases 85% or 32 had a family history of allergy where only about 26% of healthy adults have a personal or family history of allergy. Gutmann(48) believes that the cases of familial colitis may be explained on this basis. Sensitization to bacterial toxins(50) as well as to foods may produce the allergical picture.

Therefore, perhaps a few cases of chronic ulcerative colitis may be explained entirely on the basis of allergy.

RELATION OF ALLERGY TO TILSES

There is no history of hay-fever, asthma, migraine, eczema, urticaria, or spasmodic rhinorrhea in the Tilse Family. Thus, allergy is not a factor producing their disease.

Psychogenic Etiology

Sullivan(105, 106), Bodman(23), Murray(81, 80), Callander(29), and Bell(21) stress the psychogenic motivation of diarrhea. It has long been recognized that diarrhea is a common response to fear and these men point out cases giving analysis of the psychogenic origin of the diarrhea. The symptoms may be typical of chronic ulcerative colitis and the proctoscopic picture can be classical in appearance. Sullivan(106) presented 15 cases that had been diagnosed as ulcerative colitis and treated medically before coming to him with no improvement. Under psychogenic therapy alone, these patients obtained phenomenal remissions, and, although they occasionally recurred, further psychic treatment resulted in their continued improvement. In every case the patients met the stress and strain of life in an infantile manner. Murray(81) found mental conflicts concerning marriage one of the most common foundations of an anxiety diarrhea.

In reviewing the Tilse Family, however, it is seen that everyone of them was put on his own resources early in life and that most of them accomplished far more than the average individual would have been able to do. They met their tasks and problems squarely without the

slightest maladjustment. No neurotic traits could be discovered in any of them unless it was Leonard Tilse and it seems that he had ample reason to get into his morbid mental condition. Therefore, in this particular family the psychogenic factor cannot be considered as an etiological factor.

METABOLIC DERANGEMENT

A metabolic derangement has been considered by some men as the underlying factor causing the disease, but this is of more historical interest than actual present day value. Brown in 1934(24) studied 15 patients in regards to their duodenal contents thinking that the disease was due to an increased concentration of the duodenal enzymes which combined with some decrease in resistive power of the colon wall resulted in autodigestion of the mucosa producing the ulcerations. He found that there was an increase in the amount of proteolytic and amylolytic enzymes in his 15 patients and with increased peristolysis, the digestive activity of the enzymes, when they reached the cecum in those patients that had ileostomies, were just as potent as when they were secreted in the duodenum. This has been discarded, however, because of the lack of experimental investigation.

Felsen(43) demonstrated a definite hypertrophy of the Meissner(submucous) and the Auerbach(myenteric) plexuses of nerves in colitis cases with productive fibrosis, and inflammatory thickening of the intestinal wall. Therefore, he wondered if a neurogenic factor might be involved, but there has been no experimental proof to back this.

PREDISPOSING FACTORS

Larson(64) of the Mayo Clinic studied the predisposing factors in 233 cases of ulcerative colitis. Sex, nationality, and geographic distribution had no relationship with the disease. It occurred most frequently in the 3rd and 4th decades.

Out of the 233 cases 53.2% or 124 of them showed some predisposing factor in relation to the onset of the disease. These were as follows:

1. 52 of the 124 had some upper respiratory infection such as influenza, coryza, sore throat, otitis media, or sinusitis,

2. 50% had a history of local trauma or lowered resistance such as constipation, chronic use of laxatives, enemas, amebic dysentery, and hemorrhoidectomy,

3. 5% showed some relation to psychic factors,

4. and a miscellaneous group.

Exacerbations seemed to be caused by similar predisposing factors, but upper respiratory infection was seen in a larger percentage.

Upper respiratory infection is seen to be one of the predisposing factors in this family as is shown by the acute exacerbation following Arnold Tilse's fall into an icy river which was followed by an acute coryza. Constipation also seemed to be a predisposing factor in several of them.

SUMMARY

The actual cause of the disease in the Tilse Family is not known and one can only theorize as to its etiology. However, it seems to be due to an hereditary or genetic predisposition which is associated with secondary infection when the body resistance is lowered by overwork, or other disease process.

TREATMENT

The next question is what is the most expedient and effective treatment that may be offered the Tilse family for their ulcerative colitis

There have been and still are many different types of treatment that are recommended for chronic ulcerative colitis and, just as in other diseases where there are numerous treatments offered, none of them is at all specific and none produces excellent results. However, the present day prognosis for a patient with ulcerative colitis is much better than it was in former years and fairly good results are now being obtained.

Bargen (6) believes that the disease should be considered as is tuberculosis and that one should speak, not of its cure, but of its control. He believes as do many others (5, 3, 6, 7, 9, 10, 14), that treatment is primarily medical and that surgery should be reserved for complications and intractible cases.

As in tuberculosis, rest is one of the most important theraputic measures (85, 60, 66, 3, 5, 6, 7, 9, 10, 14, etc.) In the severe acute stage this should consists of quiet bed rest, but as the patient gradually improves restful exercise such as short walks, and the like should be added. However, the amount of exercise added should

always be graded and the patient should never be allowed to over exert himself. Along with this, careful nursing care should be administered. Joiner (57) recommends hot stupes, electric pads, and poultices to the abdomen to relieve abdominal pain and to act as a sedative upon bowel activity.

Occupation therapy is stressed by Pattie (89) in the treatment. She quotes Bargen from his recent book, "The Management of Colitis", as saying, "For the more chronic, although severe case without fever, restful recreation is important. By this is meant that the patient should not be kept in bed, but should have a very positive program of mild activity....This type of diversion is invaluable". Such recreation prevents the patient from continually thinking of himself and his condition. The number of trips to the bathroom while the patient is thus occupied is noticeably fewer than when he is thinking of going again. Any colitis patient who has nothing to do but wait and watch for one spasm of pain after another soon gets into a very bad nervous state. He becomes pessimistic, and his outlook on life is morbid. Consequently, diversion of thought and physical activity serve as a valuable nervous stabilizer and produce an optimistic attitude.

Chaulk powders are recommended by many (6, 40, 53, 66, 121) for their protection and absorption properties. Bargen (6) suggests the use of bismuth or tribasic calcium phosphate in amounts of grams 4-8, three to five times per twenty-four hours, or kaolin grams 30-90 in the same frequency. Howe (53) also adds barium sulphate. Eyerly and Brehaus (40) suggest the use of aluminum hydroxide in combination with kaolin. They believe that their astringent action lessens the absorption of the bacteria and their toxins, reduces the transudate from the inflamed surfaces, and that the aluminum hydroxide adsorbs the bacteria and their products. Their results in six cases were favorable, and they prove it non-toxic by experimentation on dogs. It is hard to ascertain the actual value of such protective substances, but apparently they are not harmful and they may produce favorable results.

Soper (103) has obtained very good results in two hundred fifty-two cases by the insufflation of the dry powder of bismuth directly on the mucosa. However, insufficient controls have been used to determine the exact value of such treatment. He uses a pneumatic powder blower with a 22 F. soft rubber urethral catheter. He inserts the catheter in the rectum and blows the powder directly into the colon, being careful not to over

distend the bowel by frequently allowing the gas to come back out through the catheter. He uses equal parts of calomel and bismuth subcarbonate well mixed in a mortar for the lower colon, and bismuth subgallate for the higher lesions as it is lighter. Both are astringent, adhere well, and have high antiseptic value. Such a regime may be used in all cases excepting the long chronic cases with deep ulcers, as here there is the hazard of perforation of the weak friable bowel.

Antispasmodics are advocated by nearly all men. Opium is one of the favorites (1, 6, 40, 66, 94). It may be given in the form of the camphorated tincture of opium--4 cc., or deodorized tincture of opium--5-15 minims (6). A good method to control the dosage is to give it after every alternate stool. Atropine is used by some (94) and codeine--gr ½ to 1 is used at the Mayo Clinic (6). Howe (53) uses the combination of paregoric and bismuth in the acute stages with good results. Goldstein and Samuel Weiss (46) believe that perparin hydrochloride grams 0.04 with 3-6 tablets per day, or this combined with novatropin grams 0.0015 in tablet form is the best antispasmodic. These may also be given intramuscularly and subcutaneously. Then effects appear within ten or fifteen minutes after ad-

ministrations. They show that these have a powerful antispasmodic effect on rabbits and in their cases of chronic ulcerative colitis they have proved very effective.

However, Bargen states (6), "No single drug has been found that will help more than an occasional patient. Medicines too numerous to mention, have been tried, with indifferent success in most instances; elaborate claims have been made for a few."

Other drugs that may produce some favorable effects are as follows: The Logan therapy of tincture of iodine 5-15 drops in a glass of water t. i. d. gives excellent results in occasional cases (3, 5, 7, 119). If no improvement is noted in the first week, Bargen (6) believes that it might as well be stopped. Mones and San Juan (77) in their cases obtained only indifferent results with iodine. Gentain violet in enteric tablets grains ½ may be of value when given in large enough quantities to color the stools blue (3, 5, 7, 6, 9, 53). Mercurochrome advised by Andresen and D'Albora has proved of no value in the hands of Bargen and others (3, 5, 6, 7, 71). Similarly metaphen has produced little change. Arsenic is a dangerous drug that should not be given in the stage of active bleeding as it is likely to cause an augmentation of trouble. If used at all, it should

be used in the stage of improvement as a stimulant in the form of arbarsone, treparsol, or stovarsol (3, 5, 6, 7). Davis (34) uses quinine bisulphate, gr 10, gradually increased to gr 40 according to tolerance, to check the frequency of bowel movement and to control the hemorrhage. Mones and San Juan (77) highly favor the administration of reduced iron inddoses of gram 2-4 per day. This is supported by Lupps and Schottmuller (66) who believe that it should be given in smaller doses gr 4-6 per day. Haskell (71) first advanced the use of calcium and parathormone and it has been used with favorable results by many. Both reduced iron and calcium seem valuable from the symptomatic standpoint, for these patients nearly always develop an anemia and their blood calcium and phosphorous become low. However, Bargen (3, 5, 6, 7, 8) believes that it is better to use blood transfusions which were originally suggested by Rachwalsky in small amounts of one to three hundred cc. and repeated then every four to seven days. Also immune transfusions have been recently suggested with unusually good results. Many other men support the use of transfusions and have obtained good results from them (57, 94, 103, 109). However, Mones and San Juan (77) saw no local improvement from their use. Cartwright

(30) advocates the use of Alpha Naphco Jelly and liquid. This is given in capsules 2 a. c. t. i. d. and liquid 15 drops every hour up to ten doses daily. Montague (78, 79) highly recommends the use of buffered citrates intravenously. These are given on the theory that they restore normal blood chemistry, improve capillary circulation of the intestinal mucosa, and rebuild the acid balance of the blood increasing the body's resistance to infection. Thus by improving the effeciency of the metabolic conveyor the mucosal resistance of the colon is augmented. In a series of forty-five patients he achieved marvelous results with this treatment along with the use of high vitamin diets. Out of the forty-five all but three apparently improved markedly.

It is very difficult to ascertain the value of any one drug since there is no adequate means of using controls and the drugs are always used in combination with other therapy.

Numerous solutions have been used for irrigation of the colon(3, 5, 6, 7, 9, 35, 43, 44, 46, 71, 85, 94). These include normal saline (5), neutral acriflavine 1: 4000 in normal saline (35), potassium permanganate chloramine(43), mercurochrome (46), bismuth gentian violet (46), copper sulphate 1:10,000 or azochloramid (46), silver

nitrate (85), occasionally Dakin's (85), sodium bicarbonate (101), and sometimes starch enemas. Bargen(6) feels that irrigations are of questionable value since they may irritate the colon and produce more of an inflammatory reaction than simply cleanse the mucosa as is desired. A specific example of their harmful effect is seen in the case of Arnold Tilse when he was given enemas containing corn starch, bicarbonate of soda, and powdered alum by Dr. E. G. Johnson of Grand Island in 1935. Following these enemas the patient immediately had an exacerbation of his symptoms and again began losing weight with an increase in his bowel movements. Thus, if irrigations are to be used, it seems that normal saline(6) or neutral acriflavine(6) is the best and that no irritating solution should be used at any time.

The diet is probably one of the most important measures in the regime for chronic ulcerative colitis and it should consists of a high caloric, high vitamin, non-irritating, low residue diet with an adequate amount of minerals (3, 5, 6, 7, 9, 40, 79, 85, 103). At Mayo's (111) the patient is first put on a low-residue diet as a foundation and then gradually foods are added that will increase the caloric, protein, and vitamin content. The

patient is begun on such a menu as:

Breakfast	Dinner	Supper
Cream of wheat	Beef soup	Rice, steamed
Cream	Tenderloin steak	Creamed chicken
Bacon	Baked potato	Bread, rye
Shirred egg	Bread, white	Butter
Toast	Butter	Caramel pudding
Butter	Spanish cream	Cream
Coffee	Cream	Tea
	Coffee	

Then on every second day the following additions are made, depending of course upon the extent and severity of the patient's ailment:

1. Banana, very ripe--1
2. Orange juice--¼ glass
3. Vegetable puree--2 tablespoons
4. Milk (in the form of milk toast or cream soup)--¾ glass
5. (a) Milk--2 glasses
   (b) Meat is increased by one serving
6. Fruid, bland--1 serving
7. (a) Cream added to above milk making it half and half
   (b) Tomato juice--½ glass
8. (a) Vegetable as a whole with puree being omitted, but with low residue class-- 1 serving
   (b) Lettuce, shredded--1 serving

The final diet then is a low residue, non-irritating, high vitamin, high protein, and high caloric diet as follows:

Breakfast	Dinner	Supper
Orange juice	Tomato Bouillon	Baked liver
Corn flakes with sliced bananas	Roast veal, gravy	Potato puff
	Parsley potatoes	Peach whip
Bacon and egg	Buttered carrots	Sugar cookies
Toast	Shredded lettuce	Bread
Butter	Ice cream	Butter, jelly
Milk and cream	Bread	Milk and cream
Coffee	Butter	Coffee
	Milk and cream	
	Tea	

Food is not to be taken between meals and iced desserts should be eaten slowly. No condiments such as spices, mustard, horse-radish, catsup, vinegar, and seasonings are permitted. It is also noted that in the beginning milk is not given as it is not tolerated well in most cases and is rather high in residue (6).

Sterns (104) lists the diet of chart I for chronic ulcerative colitis patients. She agrees with the May Clinic in the fundamental requirements of the diet and it is noted that her diet is smoothe with as little residue as possible and yet the diet is normal in minerals and vitamins. Residuefree diets are low in these substances, and, therefore, should not be given for more than a short interval. To supplement the diet minerals and vitamins may be given in the form of medication. It is also noted that she allows milk, but that the following foods are on her restriction list:

1. Fruits, vegetables, and whole grain cereals that contain appreciable amounts of cellulose as they tend to form gas,
2. Meats containing long fiber,
3. Concentrated sweets which ferment easily and produce gas,

COLITIS DIET--STERN

Food	Gms.	C	P	FF	Ca	P
Egg	100		13	10	.066	.180
Cheese, American	30	1	8	11	.279	210.000
Milk	960	48	32	38	1.152	.892
Cream, medium	120	5.5	3	22	.112	.096
Butter	60			52	.008	.012
Flour	4	2.5	0.5			.003
Bread, white	120	96	18	3	.054	.174
Soda crackers	36	27	3	3	.006	.036
Cereals						
Cream of wheat	175	23	3.5	0.5	.006	.037
Macaroni (cooked)	150	22	4		.006	.043
Cornstarch	10	9				
Potatoes	150	27.5	3		.021	.287
Sugar	25	25				
Cake, plain		27.5	3	4	.019	.034
Totals:		314	91	143.5	1.729	1.804

Food	Fe	A	B	C	D	G
Egg	0.0030	1980	56		96	144
Cheese, American	0.0004	750	6		6	60
Milk	0.0024	2038	107		0-50	312
Cream, medium	0.0002	880				
Butter		2166				
Flour						
Bread, white	0.0018					
Soda crackers	0.0006					
Cereals						
Cream of wheat	0.0002		2			
Macaroni (cooked)	0.0004					
Cornstarch						
Potatoes	0.0013	40	60	16		25
Sugar						
Cake, plain	0.0003	114	5			16
Totals:	0.0106					

Calories: 2911

Vitamins are given in Sherman Units.

4. Condiments and spices such as pepper, vinegar, mustard, and other sources such as broths, soups, and gravies,
5. Very hot or very cold foods, especially the latter,
6. Nuts,
7. Tea, coffee, and cocoa, which is another group allowed at the May Clinic.

Foods that are allowed in her diet are as follows:

1. Milk, which is a good source of vitamins and minerals,
2. Vegetalbes and fruits, which are not allowed at first, should be added to the diet as soon as possible. Strained tomato or orange juide may be given first, then cooked and strained vegetables and fruits. When the condition is greatly improved well-cooked, tender, young vegetables, without straining such as young beets and carrrots, tender leaves of spinach, squash, string beans, and others of like consistency are included.
3. White bread and cereals primarily add carbohydrates to the diet, whereas wholegrainbread and cereals add to the mineral and vitamin content. Therefore, it is desirable to introduce strained or

very finely ground whole grain cereals and whole grainbread as soon as possible.

4.. Meat, fish and chicken are valuable for their protein, iron, and vitamins and should be added to the diet as soon as tolerated, the more tender kinds being given first. Eggs,are a good source of protein, fat, phosphorous, iron, and some of the vitamins.

5. Butter and cream add fat to the diet and supply the fat-soluble vitamins. Tea, coffee, or cocoa should be used only in small amounts for flavoring.

Davis (34) believes that the addition of proper amounts of vitamin B and G by medication is essential and he also believes that the cause is chiefly a matter of avitaimosis. Other men, although not substantiating avitaminosis as an etiological factor, likewise include high vitamin quantities of all the vitamins in their theraputic regime (3, 53, 79, 94, 103). This may be given in the form of Brewer's yeast, halliver oil, or some of the more recent vitamin concentrates.

The nearest approach to specific therapy has been produced by Bargen of the Mayo Clinic (3, 5, 6, 7, 9, 14, 15) who has developed the Bargen's vaccine which is

an autogenous vaccine from the diplostreptococcus and the Bargen's Serum which is diplostreptococcus immunized horse serum. The serum (14) is produced by injecting graded doses of the various strains of the diplostreptococcus which are taken from fresh lesions of chronic ulcerative colitis and preserved in two parts glycerine and one part 25% sodium chloride into a horse until the horse becomes completely immunized. After the horse is immunized, he is bled seven to ten days after the last previous injection and at intervals of three to six weeks thereafter. After clot retraction the serum is tested as to agglutination and precipitation titre, and as to protective power in experimental rabbits. Finally it is proved sterile. Then in order to prevent anaphylactic reactions after frequent injections of the serum, it is further treated by adding one part serum to ten parts acidulated five percent ether in water. The reaction is kept at a pH of seven and it thus yields a modified euglobulin containing essential antibodies. This settles out in a few hours and is collected and dissolved in a mixture of glycerin and salt which is in high enough concentration to act as preservative. This is diluted with water and brought to a pH of 7.[illegible]. Thus the final product contains only about two milligrams of nitrogen in each cubic centimeter,

and, therfore, the anaphylactic reactions are not severe. It is begun in doses of one tenth cc. which are increased by one tenth cc. daily until a maximum of two or three cc. is reached.

With this treatment (10) Mayos have found that in a series of over 1500 cases only about two or three percent of cases are intractable to medical treatment where previously twenty-five to fifty percent of their cases did not respond to medical regimes. Complications now develop in only about fifteen percent of their cases where previously this too was much higher (6). Out of four hundred seventy two cases(66) seen at the Mayo Clinic up until August 1, 1931, three hundred fifty-two recovered sufficiently to resume work, two hundred fifty were symptom free, one hundred two showed seventy-five percent improvement, twenty-six showed fifty percent improvement, forty-five received insuffieient vaccine, and forty-nine showed no improvement. Of this series most of them had been treated with the Bargen Vaccine. Results with the Serum have been analogous or perhaps a little better. Of their total fifteen hundred or more cases the results have been very similar to the following representative group treated with specific serum up until April, 1937.

Grade of improvement	0	1	2	3	4	Total cases
88 cases with plus diplostreptococcus	8	10	43	23	16	88
93 cases with no diplostreptococcus	15	17	37	20	11	93

Grade 0--No improvement
1--Slight, but unsustained
2-- Moderate continuous improvement
3--Marked improvement with relief of symptoms and no recurrence to date.
4--Complete relief of symptoms

From this chart it is seen that patients that do not have the diplostreptococcus in their lesions respond, but not as well as those that do have it. Furthermore, they found that response to treatment varies inversely with the duration of the disease, and directly with its activity and severity.

Many other men have confirmed Bargen's results with the theraputic use of the serum. Lups(66), Kracke (62), Soper (103), Smith (101) all have obtained results nearly as good asBargen's, but in a smaller group of patients. However, there are others that see no value in the serum whatsoever. Kiefer (60) in a series of fifty-five cases in which he gave some of them the Bargen serum and vaccine could see no value in it. Mones and San Juan (77) believe that it has no effect, and Paulson(92) does not think that the diplostreptococcus plays a significant role in the etiology, and , therefore, believes

that it is of no value in treatment.

Another group of men believe that dysentery vaccine and immunized horse serum are of theraputic value and they believe that they obtain just as good results with them as Bargen does with his. Felsen (44), Winkelstein and Herschberger (117), Hurst (55), Crohn and Rosenak (32), and Portis (94) are some of the group that have obtained good results with antidysentery horse serum. Hurst was the original person to suggest its use. Kiefer (60) in his series of fifty-five cases could see no advantage in it, and there are many other men, including Bargen, who believe it has no theraputic value. As a whole this group of individuals has not tried it on nearly as large a group of patients as has Bargen and their work has been less substantiated.

Bassler (17) who emphasizes the symbiotic relationship of bacteria in the role of etiology uses autogenous vaccine made from each individual's stools with apparently good results. Howe (53) also uses it in conjunction with Bargen's vaccine and serum.

Schwartyman and Winkelstein (100) have used anti-B. Coli horse serum of high neutralization titre, as determined by local skin reactivity to B. Coli, and in eighteen out of twenty-one cases have obtained satisfactory

clinical improvement.

Bacteriophage has been used by some and especially by Macneal, Frisbee, and Applebaum (70). In a small series of seven cases six were given good improvement while one was not helped at all. They consider the bacteriophage relatively harmless and although the results are not phenomenal, it may be of value in certain cases. They are broad-minded enough to realize that the results may be actually due to action of the phage on the organisms, from psychic encouragement to the patient or from more careful observation and enthusiastic clinical care.

Antivirus treatment has been advanced by Oesterlin, Johnson, Kinseh, and Willett (87). In a series of seventeen cases all but one recovered completely and he died of peritonitis. All of these patients were ambulatory except two who were hospitalized. In all of them the bleeding gradually stopped in from six to fifteen days. However, exacerbations occurred so they also advise the removal of foci infection to prevent these recurrences. The antivirus is prepared by taking the bacteria from the stools and inoculating a large flask of plain broth. This is left for eight days in an incubator at 37 degrees Centigrade and then is filtered

though a Berkefield filter. The filtrate is heated to one hundred degrees centigrade for five minutes and it is then ready for use. Although they do not have a very large series of cases, they have performed much experimentation upon rabbits and have obtained some rather convincing results. They found that after injection of the bacteriophage into the peritoneal cavity resulted in immunization of the rabbit to that bacteria for which the bacteriophage was specific and which in this case was bacillus pyocyaneus, a very virulent bacterium to rabbits. Lethal doses injected into these immunized and control rabbits resulted in all of the control rabbits dying and only the immunized rabbits withstanding the injections. The phage was found to be specific for that and only that bacterium and subcutaneous and intravenous attempts at immunization failed.

Thus we see that although several so-called specific measures have been suggested none of them has been adequately tested. There is no means of running human controls and the only way of determining the value of any such measure is to use it in a large number of patients and then some reliable information can be derived. Bargen of Mayo's is the only one who has done this, and although his serum and vaccine are not phenomenal in their results, they appear to have some value in most cases.

Kiefer conclusively shows that anyone's results vary inversely with the severity of the cases. In mild cases any treatment will achieve marvelous results, while the same treatment used on sever, fulminating cases seems to do nothing. In fifty-five cases he graded the patients as to Grade I, if there was no toxemia; GradeII, if there was no toxemia, but irreparable colon damage; and, Grade III, if there were toxic signs such as fever, leukocytosis, and the like. In group III consisting of sixteen patients he obtained satisfactory results in seventy-six percent and unsatisfactory in only twenty-four percent. Satisfactory results were considered to be a definite improvement without exacerbations, and unsatisfactory results only temporary or no improvement. Thus any one person's results depends a great deal upon the severity of the pathology.

Crohn and Rosenak (32) believe that the benefits from serums and vaccines are entirely due to the febrile reaction accompaning the anaphylactic shock. In his cases he obtained just as good results from typhoid vaccine as he did from antidysentery serum, and the greater the febrile reaction the better the response. He also points out that other men such as Kantor (59) noted that his results with transfusions were best when

the transfusion was definitely accompanied by a febrile reaction. Andreson (32) obtained analogous results with mercurochrome and Bargen has also noted that his results were best when his vaccine casued some fever response. Crohn and Rosenak obtained the best results, however, from the use of neutral acriflavin 1:4000, irrigations in their series of ninety private patients.

Lastly, it is advisable to give treatment for amoebiasis if there is any question at all concerning whether or not the patient might have a chronic ameebiasis (5, 44, 46, 85, 110). Felsen (43) outlines the useful drugs in the treatment as follows:

1. Emetine hydrochloride--gr ½ by tablet every evening and every morning by subcutaneous injection for a period of twelve days and repeat with relapses. This is the most frequently used drug.
2. Chiniofon--fr 7½ by mouth t. i. d. for ten days. This also may be used in daily enemas of two hundred cc. two percent solution to be retained as long as possible. This drug is advantageous since it is less toxic than emetine hydrochloride and yet produces nearly as good results.
3. Acetarsone--gr 4 by mouth t. i. d. daily for one week and repeated if necessary after one weeks

rest. This is used after courses of emetine hydrochloride for the chronic carriers.

4. Vioform--gr 10 by mouth daily for tendays in the form of three enteric coated capsules. It has low toxicity.
5. Carbarzone--gr 4 in gelatin capsules b. i. d. for tendays. It maybe used in the acute stages along with emetin hydrochloride and it is especially good in the chronic cases.
6. Oxygen insufflations into the colon aids also becasue the amoeba like oxygen and thus tend to remain at the surface.

Surgery today is used much less frequently than in former years due to the better success of the medical treatments. However, surgery is definitely indicated (6, 37, 85):

1. In cases that are intractable to medical treatment(32),
2. For complications of neoplasm, polyposis, stricture, perirectal abscesses (77), perforation, or massive rectal hemorrhage.

In the first group McKittrick and Miller (85) consider massive hemorrhage; fever especially if accompanied by rising pulse, nausea, and vomiting; inability to eat especially if accompanied by a serum protein below

five and one half percent; abdominal pain, increasing distention, or tenderness along the course of the colon; continued bloody diarrhea with secondary anemia when there is no improvement in the anemia from four transfusions of five or six hundred cc of blood at four to seven day intervals.

Complication occurred in only fifteen percent of the cases seen at the Mayo Clinic,[3rd] only two to three percent were intractable to medical treatment. Thus, the need for operation is less frequent than in previous years when it was the only really successful means of treatment.

Preoperatively (85) the patient should have repeated blood transfusions to bring the blood plasma to a more normal physiological condition, intravenous fluids (99) to prevent dehydration, and lastly he should for twenty-four hours prior to the operation be placed on a non-residue diet. Sodium ricinoleate or vaccines injected intraperitoneally may be of some value (110).

The operations of choice are ileostomy, colectomy, and removal of foci of infection (6, 31, 32, 10, 37, 66, 85). Appendicostomy, and cecostomy are no longer considered adequate.[3rd]

Two different types of ileostomy are performed: the single barrel inwhich the distal portion of the bowel is inverted and only the proximal portion is brought through the incision for a permanent fistula, and the double barrel (31, 110), in which both portions of the bowel are brought through the incision to the outside. The advantage of the single barrel is that it is easily resected if a future colectomy is going to be performed (31), but Cattell and Trout (31, 110) believe that the double barreled type should be performed because of the danger of a colonic stricture in the single barrel type.

The technique of the operation consists of a right rectus incision and the isolation of the ileum. Cattell (31) then divides the ileum at a point six to eight inches proximal to the ileocecal valve becasue in twenty percent of the acute cases the terminal portion of the ileum is involved, but Trout (110) divides the ileum as close to the ileocecalvalve as possible. The ileum is severed by means of the cautery, a clamp applied to the proximal end,and it is brought out through the incision. In the Bargen (10) and Dixon (32) single barrel type the distal ileum is tied and iverted into thececum. In the double varrel of Gattell (31), however, it is brought

out through the incision along with the proximal end. The proximal ileum (110) is placed at the lower end of the incision and if necessary the mesentery is attached to the parietal peritoneum by means of a few number 0 catgut sutures, and the incision is closed around the intestine. Tincture of iodine painted around the bowel will aid in the early formation of adhesions between the intestine and the abdominal wall, which will thus prevent retraction of the intestine back into the perioneal cavity. Therefore, no sutures need be taken in the intestine. The clamp (10) is left on the ileum for four or five days after which it automatically becomes detached by pressure nedrosis of the end of the intestine. Twenty-four hours following the procedure the intestine is punctured by cautery immediately below the clamp and, thus, gases and liquids may escape. Moreover, with this Mikuliza exteriorization like operation the wound is kept from becoming contaminated and infected until it has begun to heal. Cattell (31) uses another refinement in which the distal ileum is brought out through a stab wound, providing the patient is in good condition, and this is located as far away from and above the permanent fistula as possible (see diagrams). Trout (110) uses

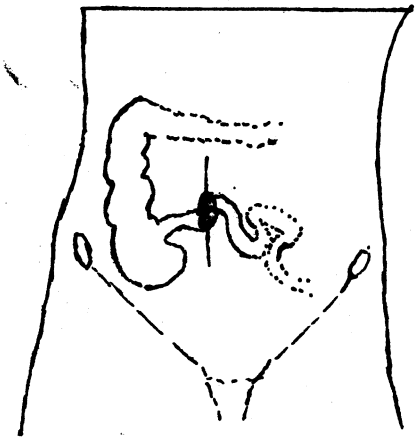


Diagram 1: Usual double barrelled ileostomy.

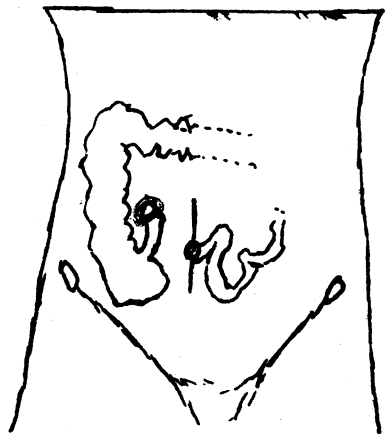


Diagram 2: Cattell's refinement of bringing distal end through a separate stab wound.

still another procedure where he inverts the distal stump into the cecum and insures prevention of colonic stricture by bringing the cecum out through a stab wound.

Ileostomy is accompanied (10) with high risk becasue there is danger of perforation of the highly inflammed ulcerated bowel, so, therefore, all exploratory manipulation must be omitted and the bowel handled as gently as possible. The mortality, even then, is high. McKittrich and Miller (85) report twenty cases operated by two different surgeons inwhich the mortality was only fifteen percent. However, in a larger series of fifty-five cases with eleven different operators the mortality was thirty-five percent. Crohn and Rosenak (32) had a

mortality of thirty-three and one third percent with their ileostomies, but they believe this a little high since only patients in poor condition came to surgery. One should recognize that ileostomy is not a curative procedure, but in most instances striking improvement results.

Postoperatively (110), there is marked loss of fluids and the blood chloride level should be maintained by the daily use of intravenous injections of normal saline and to alleviate starvation dextrose also may be added. Then, periodically the patient should dilate the opening of the ileostomy with his finger for several weeks afterward to prevent stenosis.

Before the patient leaves the hospital a colostomy bag (110) is fitted to the abdominal wall. There are many such bags, but as a rule, the patient finds that the simpler the apparatus the less the discomfort he has. Trout uses one that consists of a broad canvas belt that goes around the body and has a hole about four inches in diameter in it which is located over the site of the ileostomy. Around this hole is a steel ring in which canvas "hats" fit to collect the intestinal discharge. These "hats" have a diameter of four inches and a rim around the crown of about two inches. The patient places the "hat" over the ileostomy and then puts the

crown of the hat through the hole in the canvas belt. Thus, the hat is pressed comfortably against the abdominal wall. Toilet paper is put in the "hat" and the patient stays reasonably clean and free from odors. As time goes on the character of the stools becomes more solid and, therefore, somewhat easier to handle and the functioning of the artifical anus becomes more rythmical.

Reestablishment of continuity (110) generally should not be considered but in some cases where the bowel has been proven to be quiescent for a period of three years it may be considered. There should be no proctoscopic or X-ray signs of residual disease, however.

If complete relief is not given by ileostomy, then a colectomy may be considered. Indications (85) for a colectomy are polyposis with or without carcinoma, recurring attacks of bleeding temperature, and malaise or associated skin infection or joint symptoms after ileostomy has had a fair trial, and lastly continued anemia, and failure to gain strength and weight with no other demonstrable cause. The ileostomy should be allowed a trial period of four months in all cases. It should be remembered that the presence of an infected bowel continues to be a possible focus of general infection as long as it remains and that not infrequently the ulcers

in the colon perforate and produce a fatal peritonitis even after ileostomy (110). • Also the continuation of the causation of future malignancy, and an actual malignancy may even be overlooked. Furthermore, strictures occasionally develop with the healing of the ulcers, and therefore, all of this must be kept in mind when considering a colectomy (110). Most men agree that the colectomy should be performed in two stages (10, 32, 31, 37, 85, 110). The colon is first resected down to the lower sigmoid region, and then after an interval of two months (31) or after the patient is again in good condition, the lower sigmoid and rectum are removed from below.

The results of colectomy are generally quite satisfactory. McKittrick and Miller (85) found that at the Massachusetts General Hospital forty-two percent later needed colectomy, but the results of subtotal colectomy were always excellent. In a series of twenty-nine patients of their own, twenty-eight had completely recovered and only one died. The latter was in very bad condition and was operated too late to be saved.

Lastly, foci of infection should be removed to prevent recurrences and rectal fistulae and perirectal abcesses should be drained (10). However, fistulectomy should never be undertaken until the lining of the intestine

has healed, because of the danger of a recrudescence.

It is interesting to note that in one of our cases, A. W. Tilse, the symptoms followed a hemorrhoidectomy. Moltke (75, 76) noted this also and Howe (53) has noted several cases in which a hemorrhoidectomy was done to treat rectal bleeding when chronic ulcerative colitis was the underlying cause. He has found likewise that a hemorrhoidectomy generally results in an acute exacerbation of chronic ulcerative colitis and in his series one death occurred one month after the hemorrhoidectomy from a very severe colitis. Therefore, it is advisable that sigmoidoscopy be done routinely on all cases before hemorrhoidectomy.

SUMMARY

In summary the treatment that would be recommended for the Tilse Family is as follows.

They should be treated medically until either complications develop, or they are proven to be definitely intractable to the medical treatment. Such treatment should consist of:

1. Rest and then restful recreation with occupation therapy of interesting nature to keep the patient

happy, comfortable, and optimistic.

2. A high caloric, high vitamin, non-irritating, smooth diet.
3. Antispasmodics such as opium or perparin hydrochloride given over a long period of time.
4. Some protective powder such as either kaolin or bismuth subnitrate by mouth.
5. Irrigations should not be used often if at all and should only consist of normal saline or occasionally neutral acriflavine.
6. Bargen's vaccine or serum, and autogenous vaccines should be used.
7. Antidysentery serum if the patient has a positive agglutination to one of the dysentery bacilli, which is not known.
8. Antivirus of bacteriophage might be worth a trial if the above treatment fails.
9. Frequent small transfusions and intravenous buffered solutions.
10. Vitamin medication with largest quantities of Vitamin B and G.and antianemia therapy.
11. Removal of foci of infedtion.

Then if the patient failed to improve or complications developed an ileostomy should be done which may later be

followed by a colectomy if the patient continues to be bothered.

Exacerbations tend to occur following upper respiratory infections so after improvement the patient should be careful not to expose himself any more than necessary to colds and other infections, and the Bargen's serum, as well as a slightly restricted diet, should be continued for some time.

If symptoms of obstructive ileitis occur, surgical removal of the ileum should be done.

REFERENCES

1. Andresen, A. F.: Gastro-intestinal manifestations of food allergy, Med. J. and Rec., 122:271-275, Sept. 2, 1925.

2. Arrismith, W. W.: Personal communications.

3. Bargen, J. Arnold: Chronic ulcerative colitis--trends in its present day management, Am. J. Dig. Dis. & Nut., 1:190-192, May, 1934.

4. Bargen, J. Arnold: Differential diagnosis and treatment of the types of colitis, West. Virginia M. J., 29:20-27, Jan. 1933.

5. Bargen, J. Arnold: Dysentery--Its medical management, Minn. Med., 19:33-36, Jan. 1936.

6. Bargen, J. Arnold: The medical management of chronic ulcerative colitis, Proc. Roy. Soc. Med., 30:351-362, Febr. 1937.

7. Bargen, J. Arnold: Ten years experience in the treatment of chronic ulcerative colitis, Tr. Am. Gastroenterol. Ass., 36:49-60, 1933.

8. Bargen, J. Arnold, and Barker, Nelson W.: Extensive arterial and venous thrombosis complicating chronic ulcerative colitis, Arch. Int. Med., 58:17-31, July, 1936.

9. Bargen, J. Arnold, and Coffey, Robert J.: The most important feature in the management of chronic ulcerative colitis, M. Clinic North Am., 19:403-407, Sept. 1935.

10. Bargen, J. Arnold, and Dixon, Claude F.: Essential operations for chronic ulcerative colitis, Ohio State M. J., 32:650-653, July 1936.

11. Bargen, J. Arnold, and Dixon, Claude F.: Recent studies on the physiology of the human intestine: Their application to clinical problems, Rev. Gastroenterol, 3:205218, Sept. 1936.

12. Bargen, J. Arnold, and Kemble, J. W.: A study of predisposing factors in chronic ulcerative colitis, Proc. Staff. Meet. Mayo Clinic, 10:364-368, June 5, 1935.

13. Bargen, Jacob A., and Logan, Arch H.: The etiology of chronic ulcerative colitis, Arch. Int. Med., 26:818-839, Dec. 1925.

14. Bargen, J. Arnold; Rosenow, Edward C.; and Fasting, George F. C.: Serum treatment for chronic ulcerative colitis, Arch. Int. Med., 56:1039-1047, Dec. 1920.

15. Bargen, J. Arnold, and Simpson, W. C.: Chronic ulcerative colitis--Factors influencing its response to specific treatment, Ann. Int. Med., 10;1551-1555, April 1937.

16. Barnes, J. M.: Typical pellagra syndrome developing in a patient with chronic ulcerative colitis while under hospital treatment, Ann. Clin. Med., 4:552-564, Jan. 1926.

17. Bassler, Anthony: Bacteriology of ulcerative colitis, M. J. & Rec., 138:472-478, Dec. 20, 1933.

18. Bassler, Anthony: Ulcerative colitis, Interstate Med. J., 20:707-716, 1913.

19. Bassler, Anthony: Ulcerative colitis of so called non-specific type, Med. J. and Rec., 125:253-258, Febr. 16, 1937.

20. Bayard, Harry F.: Proctoscopic diagnosis of chronic ulcerative colitis, Minnesota Med., 16:487-489, July 1933.

21. Bell, Aaron: Colitis--Psychogenically motivated, J. New. & Ment. Dis., 77:587-593, June 1933.

22. Blake, A. J., and Higgs, F. W.: Statistics of ulcerative colitis, Proc. Roy. Soc. Med., 2:119-134, 1908-1909.

23. Bodman, Frank: The psychogenic background of colitis, Am. J. of M. Sc., 190:535-545, Oct. 5, 1935.

24. Brown, Philip W.: Duodenal Enzymes in chronic ulcerative colitis, Med. Clin. N. Am., 7:97-103, July 1923.

25. Brown, Philip W., and Magath, Thomas A.: Amebiasis--Diagnosis, prevention, and treatment, Minnesota Med., 18:515-526, Aug. 1935.

26. Brown, T. R.: Some observations on chronic ulcerative colitis, Ann. Clin. Med., 4:425-439, Nov. 1925.

27. Brust, John C. M., and Bargen, J. Arnold: The neoplastic factor in chronic ulcerative colitis, New England J. of Med., 210:6920696, March 29, 1934.

28. Buie, Louis A., and Bargen, J. Arnold: Chronic ulcerative colitis, J. A. M. A., 101:1462-1466, Nov. 4, 1933.

29. Callander, R. J.: Functional colitis, Southwestern Med., 13:428-433, Oct. 1929.

30. Cartwright, Emor L.: Treatment of chronic ulcerative colitis, Am. J. Dig. Dis. & Nut., 3:70-72, March, 1936.

31. Cattell, Richard B.: Colectomy for intractable ulcerative colitis, S. Clinic North A., 17:803-814, June 1937.

32. Crohn, Burrill B., and Rosenak, Bernard D.: A follow up of ulcerative colitis(non-specific), Am. J. Dig. Dis. & Nut., 2:343-346, 1935.

33. Dack, G. M.; Dragstedt, Lester R.; and Hernz, Theodore E.: Further studies on bacterium necrophorum isolated from cases of chronic ulcerative colitis, J. Inf. Dis., 60:335-355, May-June, 1937.

34. Davis, Edward Clayton: Is colitis a deficiency disease, Tr. Am. Proct. Soc., 35:93-96, 1934.

35. DeYoung, Willard: Sources of error in the laboratory diagnosis of amebiasis, J. Lab. & Clinc. Med., 21:1149-1154, Aug. 1936.

36. Dickson, W. E. Carniegie: Ulcerative colitis, Lancet 1:1006-1008, May 19, 1923.

37. Dixon, Claude F.: Surgical treatment of dysenteries, Minn. Med., 19:33-36, Jan. 1936.

38. Einhorn, Max: Chronic ulcerative colitis and its treatment, N. Y. Med. J., 117:214-218, Feb. 21, 1923.

39. Eusterman, G. B., and O'leary, P: Pellagra secondary to benign and carcinomatous lesions and dysfunction of the gastrointestinal tract, Report on 13 cases, Arch. Int. Med., 47:633-649, April 1931.

40. Eyerly, James B., and Breuhaus, Herbert C.: Treatment of ulcerative colitis with aluminum hydroxide and kaolin, J. A. M. A., 109:191-195, July 17, 1937.

41. Felsen, Joseph: Intestinal oxygenation in idiopathic ulcerative colitis, Arch. Int. Med., 48:786-792, Nov. 1931.

42. Felsen, Joseph: New clinical conceps of bacillary dysentery and relationship to ulcerative colitis, Tr. Am. Proct. Soc., 36:133-141, 1935.

43. Felsen, Joseph: A practical etiological, pathological, and clinical consideration of intestinal ulceration, Am. J. Dig. Dis. & Nut., 1:297-305, July 1934.

44. Felsen, Joseph: The relationship of bacillary dysentery to distal ileitis, chronic ulcerative colitis, and non-specific intestinal granuloma, Ann. Int. Med. 10: 645-669, Nov. 1936.

45. Garvin, J. D.: Relation of focal infecti on to gastro-intestinal disease, Penn. M. J., 33:616-619, June, 1930.

46. Goldstein, Hyman I.: The management of idiopathic ulcerative colitis, so-called mucous colitis, and spastic conditions of the gastrointestinal tract, 3:150-157, June 1936.

47. Granet, Emil: Intestinal tuberculosis, Am. J. Dig. Dis. & Nut., 2:209-219, 1935.

48. Gutmann, Rene A.; Tzanck, Arnault; and Arnous, Jean: Les Intolerances coliques, Presse Med., 44:917-920, June 6, 1936.

49. Hanes, Frederic M., and McBryde, Angus: Identity of sprue, nontropical sprue, and celiac disease, Arch. Int. Med., 58:1-16, July 1936.

50. Hare, Dorothy C.: The allergic factor in the etiology of non-specific colitis, Lancet 2:767-768, Oct. 5, 1935.

51. Hare, Dorothy C.: Non-specific colitis, Practitioner, 133:705-716, Dec. 1934.

52. Henry, S. W.: Emotions and digestive functions, J. Am. Dietet. Ass., 3:19-23, June, 1927.

53. Howe, H. F.: Ulcerative colitis, etiology and management, Ohio State M. J., 31:672-675, Sept. 1935.

54. Hurst, Arthur F.: Discussion of the diagnosis and treatment of colitis, Proc. of the Roy. Soc. of M., 20: 367-380, Nov. 23, 1936.

55. Hurst, Arthur F.: Ulcerative colitis, Guy's Hosp. Reports, 71:26-29, Jan. 1921.

56. Johnson, E. G.: Personal Communications.

57. Joiner, Hartwell: Chronic recurrent migratory ulcerative colitis of the (Bargen) diplostreptococcus infection type, J.M. A. Georgia, 23:3-7, Jan. 1934.

58. Jones, C.M.: Peripheral complications of ulcerative colitis, Med. Clin. N. Am., 16:919-928, Jan. 1933.

59. Kantor, J. L.: Diarrhea, Am. J. Dig. Dis. & Nut., 2:1-7, March, 1935.

60. Kiefer, Everett D.: Clinical results in the medical treatment of chronic ulcerative colitis, Am. J. Dig. Dis. & Nut., 3:56-59, March 1936.

61. Kiefer, Everett D.: The diagnosis of chronic ulcerative colitis, New England J. of M., March 1, 1934.

62. Kracke, Roy R.: Chronic ulcerative colitis--Etiology, South. M. J., 23:785-789, Sept. 1930.

63. Larimore, Joseph W.: Chronic ulcerative colitis--Observations on treatment by diet, Trans. Am. Gastro-Enterol. Assn., 30:298-318, 1927.

64. Larson, L. M.: Predisposing factors in the etiology of chronic ulcerative colitis, Proct. Staff. Meet, Mayo Clinic., 6:241-244, April 22, 1931.

65. Lockhart-Mummery: Diseases of the rectum and colon, pp. 412-448, London, Bulliere, Tindal and Cox, 1923.

66. Lups, Sibrand: Vaccine therapy in ulcerative colitis, (Transulated by Baker, Abel J.), Am. J. Dig. Dis. & Nut. 2:65-90, 1935.

67. Mackie, Thomas T.: A bacteriologic, roentgenologic, and clinical study of ulcerative colitis, Am. J. Dig. Dis. & Nut., 1;466-471, Sept. 1934.

68. Mackie, Thomas T.: The deficiency factor in colitis, Tr. Am. Proct. Soc., 35:97-99, 1934.

69. Mackie Thomas T.: Food allergy in ulcerative colitis, J. Am. Dietet. Assn., 14:177-182, March, 1938.

70. MacNeal, Ward J.; Frisbee, Frances C.; Applebaum, Martha: Bacteriophages in chronic colitis of undetermined causation and in intestinal fistulas, Arch. Surg., 29:748-758, Nov. 1934.

71. Manson-Bahr, Phillip: Differential diagnosis of diseases of the colon(dysentary and colitis), Lancet, 1:830-834, April 11, 1936.

72. Mayo, C. W., and Zellhoefer, H. W. K.: Ileosigmoidostomy for chronic ulcerative colitis, Proc. Staff Meet. Mayo Clinic, 11:797-800, Dec. 9, 1936.

73. Miller, D. K., and Barker, W. Haley: Clinical course and treatment of sprue, Arch. Int. Med., 60: 385-414, Sept. 1937.

74. Minick Clarence: Personal communications.

75. Moltke, Otto: Familial occurrence of non-specific suppurative coloproctitis, Acta Medica Scandinavica, Supp. 78:426-432, 1936.

76. Moltke, Otto: Familial occurrence of suppurative colitis, Klinische Wchenschrift, 15: 124-126, Jan. 25, 1936. (Transulated through the courtesy of Jack E. Maxfield.)

77. Mones, F. Gallart, and Sanjuan, P. Domingo: Colitis ulcerosas graves no ambianas etiologia diagnostica y treatmenta medica, (Abstracted by J. Arnold Bargen, and A. E. M. Ferreira), Am. J. Dig. Dis. & Nut., 4: 247-250, June 1937.

78. Montague, J. F.: A new and promising treatment for chronic ulcerative colitis, Med. Rec., 140:670-671, Dec. 19, 1934.

79. Montague, J. F.: Treatment of chronic ulcerative colitis by buffered citrates, Med. Rec., 143:101-103, Febr 5, 1936.

80. Murray, Cecil D.: A brief psychological analysis of a patient with ulcerative colitis, J. Nerv. & Ment. Dis., 72:617-627, Dec. 1930.

81. Murray, Cecil D.: Psychogenic factors in the etiology of ulcerative colitis and bloody diarrhea, Am J. M. Sciences, 180:239-248, Aug. 1930.

82. McCoy, George W., and Hardy, Albert U.: The clinical diagnosis of amebic dysentery, J. A. M. A., 107:1357-1359, Oct. 24, 1936.

83. McGrath, B. R.: Personal communications.

84. McGrath, W. W.: Personal communications.

85. McKittrick, Leland S., and Miller, Richard H.: Idiopathic ulcerative colitis, Ann. Surg., 102:656-673, Oct. 1935.

86. Nicholls, Edith E: The incidence and biological characteristics of the hemolytic bacillus coli in the intestinal tract of patients with chronic ulcerative colitis, Am. J. Dig. Dis. & Nut., 2:709-713, Febr. 1936.

87. Oesterlin, E. J.; Johnson, A. W.; Kinsey, Jack; and Willett, Thomas: Antivirus treatment of ulcerative colitis, Wisconsin M. J., 34:538-545, Aug. 1935.

88. Overstreet, Sam A.; Differential diagnosis and treatment of chronic colitis, Kentucky M. J., 31:96-104, Febr. 1933.

89. Pattee, Gladys: Experience at the Mayo Clinic with occupational therapy for certain chronic conditions, Occup. Therapy, 16:125-128, April 1937.

90. Paulson, M.: Chronic ulcerative colitis with reference to a bacterial etiology, Archieves of Int. Med., 41:75-96, Jan. 1928.

91. Paulson, Moses: Intracutaneous responses, comparable to positive frei reactions with colonic exudate from chronic ulcerative colitis cases with positive frei tests, Am. J. Dig. Dis. & Nut., 3:667-673, 1936.

92. Paulson, Moses: The present status of idiopathic ulcerative colitis with special reference to etiology, J. A. M. A., 101:1687-1694, Nov. 25, 1933.

93. Penner, A.: Possible relationship of bacillary dysentery to non-specific colitis, Am. J. Dig. Dis. & Nut., 3:740-743, Dec. 1936.

94. Portis, Sidney A.: Treatment of ulcerative conditions of the colon, Med. Clin. North Am., 18:1319-1330, March 1935.

95. Rafsky, Henry A., and Manheims, Perry J.: The significance of the Bargen Organism as an etiological factor in ulcerative colitis, Am. J. M. Sc., 183:253-256, Febr. 1932.

96. Rankin, Fred W.; Bargen, J. Arnold; and Buie, Louis A.: The colon rectum and anus, pp. 137-333, Philadelphia and London, W. B. Saunders & Company, 1932.

97. Reed, Alfred C.: Sprue--a clinical summary, Am. J. Trop. Med., 16:499-526, Sept. 1936.

98. Riesman, D.: History taking and physical examinations in digestive disorders, J. A. M. A., 90:1192-1997, June 23, 1928.

99. Rosser, Curtice: Some proctologic problems, J. Oklahoma M. A., 26:153-156, May 1933.

100. Schwartzman, Gregory, and Winkelstein, Asher: A new type of serum therapy for the treatment of non-specific ulcerative colitis, Am. J. Dig. Dis. & Nut., 1:582-583, Oct. 1934.

101. Smith, David: A note on the serum treatment of ulcerative colitis, Glasgow M. J., 120:9-13, July 1933.

102. Snell, A. M., and Bumpus, L. D.: Unusual deficiency syndrome secondary to duodenal occlusion and ulcerative colitis, Minn. Med., 14:336-340, April, 1931.

103. Soper, Horace W.: Treatment of ulcerative colitis, South. M. J., 29:901-904, Sept. 1936.

104. Stern, Frances: Applied dietetics, Baltimore, The Williams & Wilkins Company, 1936.

105. Sullivan, Albert J.: Emotion and diarrhea, New England J. Med., 214:299-305, Febr. 13, 1936

106. Sullivan, Albert J.: Psychogenic factors in ulcerative colitis, Am. J. Dig. Dis. & Nut., 2;651-656, Jan. 1936

107. Synhorst, A. P.: Personal communications including office records and St. Francis Hospital charts at Grand Island, Nebraska.

108. Tollman, J. Perry: Personal communications.

109. Thorlaksen, P. H. T.: Ulcerative colitis, J. Canad. Med. Assoc., 19:656-659, Dec. 1928.

110. Trout, Hugh H.: Surgical treatment of ulcerative colitis, Virginia Med. Monthly, 63:1-5, April 1936.

111. Victor, Mary: Diet Manual, Rochester, Minn., St. Mary's Hospital, pp. 96-98, 1934.

112. Wallis, F. C.: Surgery of colitis, Brit. Med. Jour., 1:10-13, Jan. 2, 1909.

113. Watson, E. A.: Personal communications including a review of office records.

114. Weber, Harry M.: The roentgenologic identification of commonly encountered chronic ulcerative diseases of the colon, Am. J. Roentgenol., 30:488-496, Oct. 1933.

115. Weber, Harry M.: Roentgenologic manifestations of diseases which have dysentery as a prominent symptom, Minnesota Med., 19:23-39, Jan. 1936.

116. Weiss, Emil, and Arnold, Lloyd: A complement fixation test for amebiasis with an increased antibody content, Am. J. Dig. Dis. & Nut., 4:282-287, July 1937.

117. Winkelstein A., and Herschberger, C.: Studies on the relation of non-specific ulcerative colitis to bacillary dysentery with particular reference to the dysentery bacteriophage, Am. J. Dig. Dis. & Nut., 2:408-411, Sept. 1935.

118. Winkelstein, Asher: Etiology and therapy of ulcerative colitis, Am. J. Dig. Dis. & Nut., 3:839-844, 1936-1937.

119. Woodruf: Personal communications including a review of hospital charts.

120. Yoemans, F. C.: Chronic ulcerative colitis, J. A. M. A., 77:2043-2048, Dec. 24, 1921.

121. Yoemans, Frank C.: Proctology, pp. 276-299, New York & London, P. Appleton & Co., 1929.