# Diarrhea

Reza Malekzadeh
Professor of Medicine
DDRC/TUMS
Lecture for IAGH
Ordibehesht 1405

# Diarrhea

- Is both a symptom and a sign.

# Diarrhea As a symptom

- It is whatever the patient says it is: a decrease in consistency, an increase in the number or volume of bowel movements, or any combination thereof.

# Diarrhea as a sign

- Diarrhea is an increase in stool weight (or volume) of more than 200 g or ml) per 24 hours in a person on a Western diet (In Iran 270gm).

# Acute/Chronic Diarrhea

- Acute when it lasts less than two or three weeks , is frequently caused by an infectious agent, is usually self-limiting, and often resolves without treatment.
- Chronic when it lasts more than two or three weeks.
- Chronic diarrhea has multiple causes.

# osmotic / secretory

- It is considered osmotic if luminal substances are responsible for the induction of the fluid secretion.
- It is considered secretory if endogenous substances (often referred to as “secretagogues”) induce fluid secretion that persists even when the patient is fasting.

# Effect of a fasting on stool output

- When diarrhea ceases with fasting, a dietary nutrient is likely to be the cause (malabsorption off CHO or Fat).
- If diarrhea persists unabatedly with fasting, a dietary nutrient is not likely to be the cause.

# Stool fat

- **Normally, less than 7 g of fat per day is excreted by persons consuming 100 g of fat per day.**
- **Diarrhea alone may be responsible for an increase in fat excretion of up to 11 g per day**
- **Greater rates >11gm/day of fat malabsorption can be explained only by one or more defects in fat digestion and absorption,**

# Regulation of Absorptive and Secretory Processes in the Intestine

Secretory processes generally occur in crypt cells, whereas absorptive processes are located in villous cells

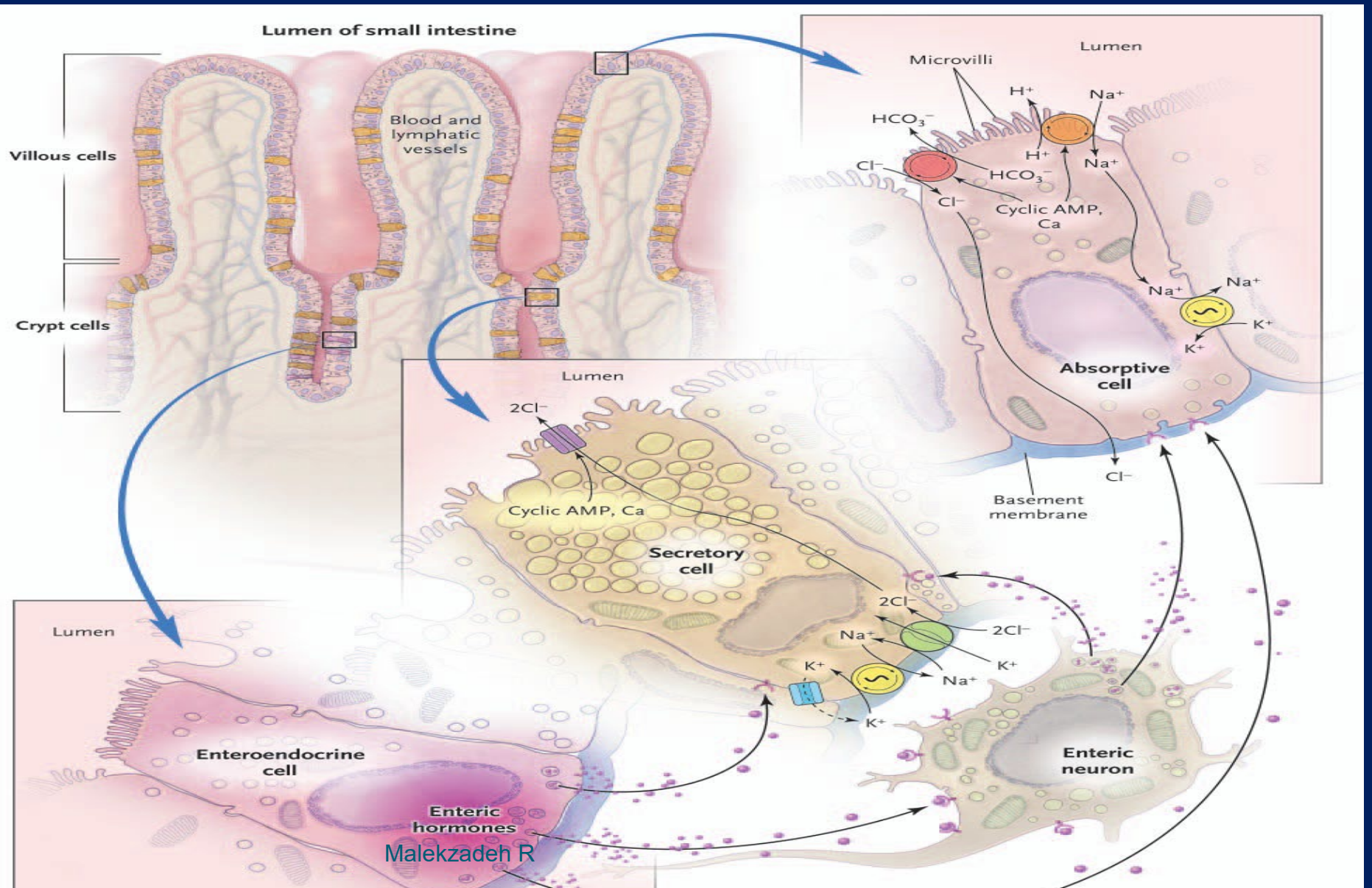
- Enteroendocrine cells are sparse but are present in the crypt.
- Almost all diarrheal disorders are associated with net fluid secretion.

# Secretary Diarrhea

- Secretary Diarrhea is most often secondary to the stimulation of active chloride secretion and to the inhibition of active absorption of sodium and chloride (by messengers such as cyclic AMP) which involves the coupling of sodium–hydrogen exchange and chloride–bicarbonate exchange.

- Absorptive and secretory processes are regulated by both the enteric nervous system and enteric hormones, although little is known about the role of enteric hormones in vivo.

# Regulation of Absorptive and Secretory Processes in the Intestine.



# LUBIPROSTONE: EASING THE STRAIN OF CONSTIPATION

- A drug that works by activating type 2 intestinal chloride channels (CLC-2) to increase the intraluminal chloride concentration which, in turn, increases fluid secretion and ultimately encourages bowel movement (BM).

# 5 well characterize Congenital Diarrheal Disorders.

| Syndrome | Defective Transport Mechanism | Mutated Gene |
|---|---|---|
| Congenital chloride diarrhea | Chloride–bicarbonate exchange | *DRA* |
| Glucose–galactose malabsorption | Glucose-stimulated sodium absorption | *SGLT1* |
| Congenital sodium diarrhea | Sodium–hydrogen exchange | *NHE3* |
| Congenital bile-acid diarrhea | Sodium-dependent bile-acid absorption | *ABAT* |
| Congenital lactase deficiency | Lactase–phlorizin hydrolase | *LCT* |

# Chronic Diarrhea

- Increase Stool Frequency >3 times a day
- Increase stool Liquidity.
- More than 2 weeks duration
- Increase stool weight >200-250 gm/day

# Causes of Chronic Diarrhea in 100 Subjects

| Cause | Percentages |
|---|---|
| Celiac disease | 19 |
| Crohn's disease | 16 |
| Lymphoma | 9 |
| Idiopathic causes | 9 |
| Tuberculosis | 6 |
| Eosinophilic Gastroenteritis | 5 |
| Bacterial Overgrowth | 5 |

Shahbazkhani , Malekzadeh R., Sotoudeh M. et al.
European Journal of Gastroenterology 2004

# Causes of Chronic Diarrhea 2

| Cause | Percentages |
|---|---|
| Immunodeficiency Syndrome | 4 |
| Chronic pancreatitis | 3 |
| Miscellaneous | 23 |

Shahbazkhani , Malekzadeh R., Sotoudeh M. et al.
Europian Journal of Gastroenterology 2003

# Miscellaneous causes of chronic diarrhea in 23 of 100 patients studied

| Causes | Number of patients (%) |
|---|---|
| Collagen vascular disease | 2 (2) |
| Strongyloides Sterocolaris | 2 (2) |
| Thyrotoxicosis | 2 (2) |
| Short bowel syndrome | 2 (2) |
| Behcet's disease | 2 (2) |
| Intestinal lymphangeictasia | 2 (2) |
| Giardiasis | 2 (2) |
| Amyloidosis | 1 (1) |
| AIDS enteropathy | 1 (1) |

# Miscellaneous causes of chronic diarrhea in 23 of 100 patients studied (cont.)

| Causes | Number of patients (%) |
|---|---|
| Cystic fibrosis | 1 (1) |
| Laxative abuse | 1 (1) |
| Drug induced (colchicine) | 1 (1) |
| Superficial spreading small bowel adenocarcinoma | 1 (1) |
| Carcinoid tumor | 1 (1) |
| Chronic Mesenteric Ischemia | 1 (1) |
| Total | 23 |

Shahbazkhani , Malekzadeh R., Sotoudeh M. et al.
Europian Journal of Gastroenterology 2003

## Sign and Symptoms in 20 Celiac Patients with Diarrhea in Tehran

| Symptoms | Number (%) |
|---|---|
| Abdominal discomfort and bloating | 12 (63.2) |
| Weight loss | 10 (52.6) |
| Nocturnal diarrhoea | 9 (47.4) |
| Nausea | 8 (42.1) |
| Vomiting | 6 (31.6) |
| Oral aphthus ulcer | 4 (21.1) |

Shahbazkhani, Malekzadeh, Sotoudeh et al.
Europian Journal of Gastroenterology 2003

# Diarrhea

- Chronic/Acute
- Small Bowel/Large Bowel.
- Organic /Functional

# Chronic Diarrhea

- Bloody/Non-bloody
- Weight loss
- IBD/IBS

# Case 1

- 34 years old housewife presented with RLQ abdomina pain and diarrhea (6 times per day) Since 2 months ago.

No other pertinent finding in history.

Diarrhea is very severe and she cannot do her daily activity and was has consulted 5 different physician during last 2 months. No weight loss.

PE=normal except for pain on palpation of abdomen with soft nontender abdomen

Paraclinical Investigation=

CBC,chemistry panel ,U/A.op/oB=neg.

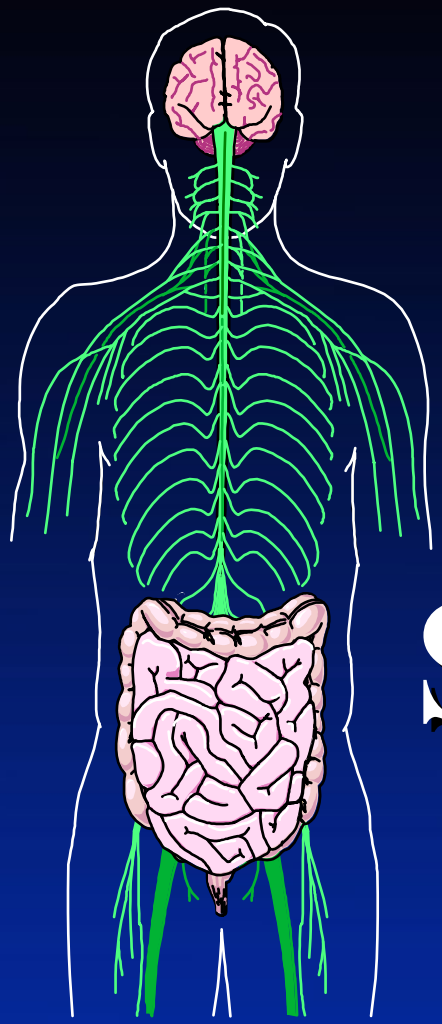
UGIE+SIGMOIDOSCOPY=NORMAL

SBS=NL.









# Irritable Bowel Syndrome

# Proposed New Subtyping Based on Stool Consistency Alone

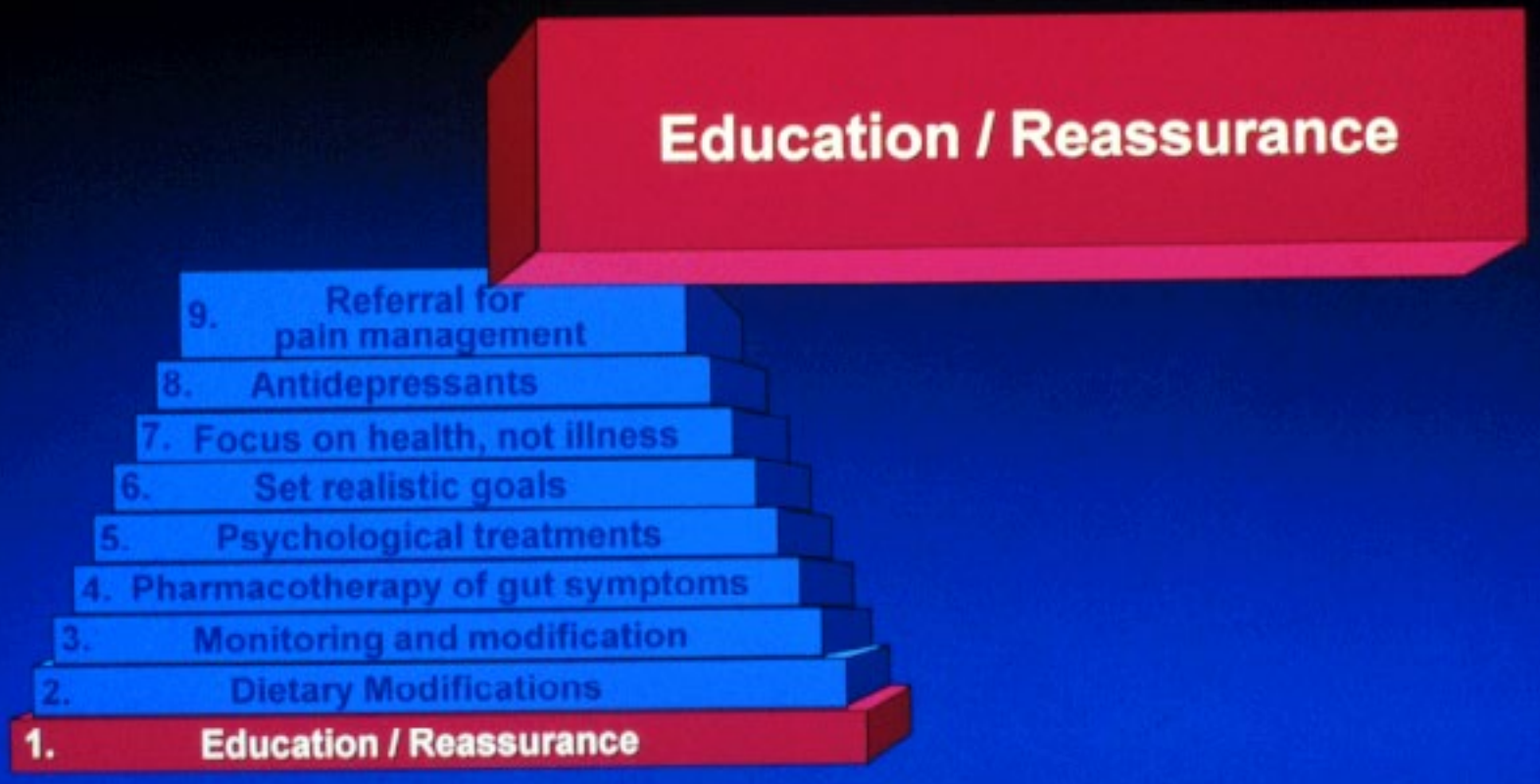
- IBS with constipation - IBS-C
- IBS with diarrhoea - IBS-D
- IBS mixed type - IBS-M
- (IBS unsubtyped - IBS-U)

- IBS-mixed : patients with both hard & loose stools over periods of hours or days

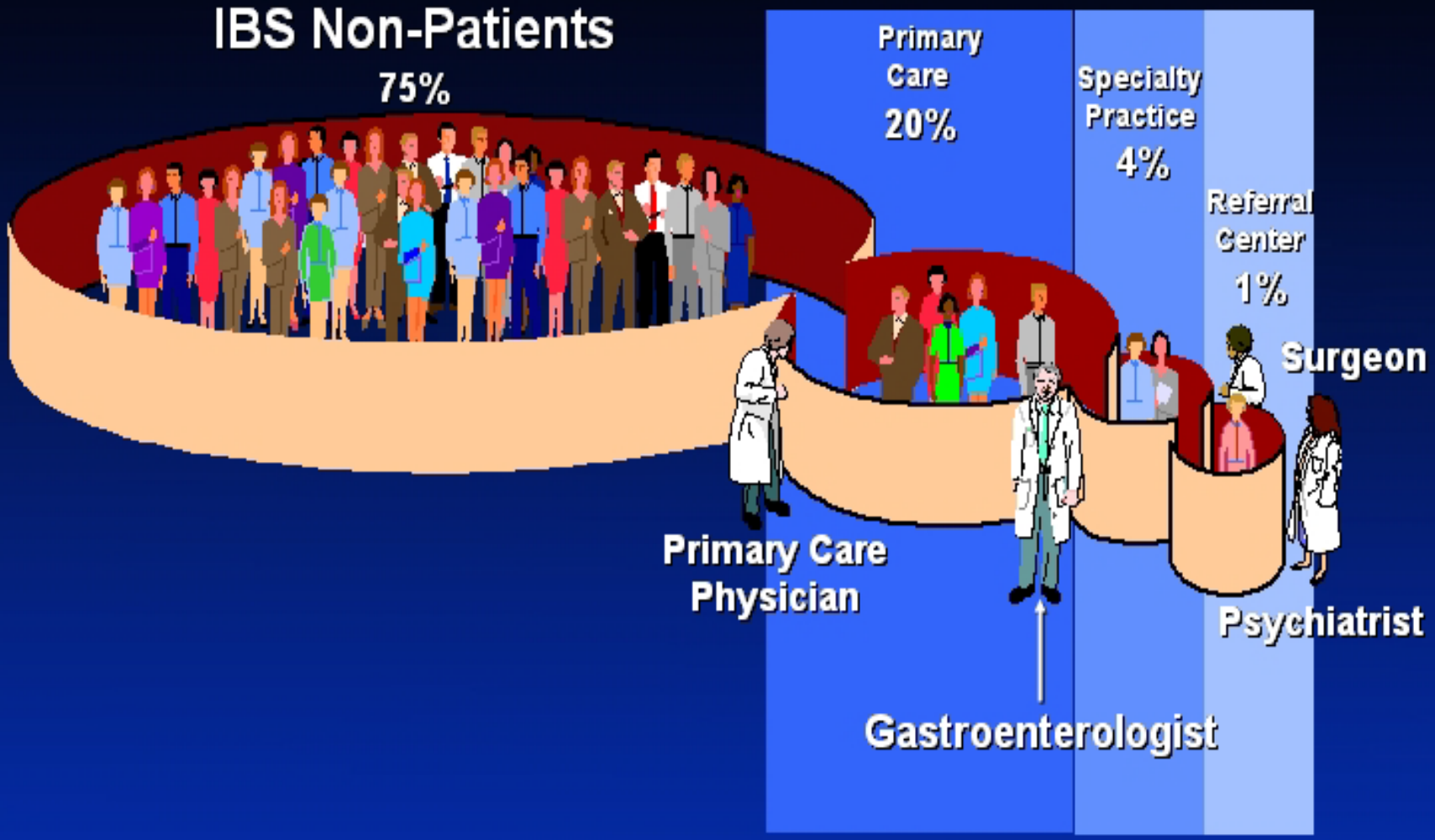
# Case Presentation

- 71 years old female housewife presented with chronic non-bloody diarrhea of >10 years duration, her weight remain low in the range of 38-41 during her life.
- No history of abdominal pain but she suffered from flatulence and couldn't tolerate milk.
- She was seen by many doctors in Iran and USA and was told to have IBS treated with loperamide with partial response .

## IBS - Treatment Approach



# Self Selection Into Clinical Practice




Drossman DA, Thompson WG., Ann Intern Med. 1992; 116:1009

Alimentary Pharmacology & Therapeutics

# Clinical trial: the effect of amitriptyline in patients with diarrhoea-predominant irritable bowel syndrome

H. VAHEDI, S. MERAT, S. MOMTAHEN, A. S. KAZZAZI, N. GHAFFARI, G. OLFATI & R. MALEKZADEH

Digestive Disease Research Center, Shariati Hospital, Medical Sciences/University of Tehran, Tehran, Iran

Correspondence to:
Dr H. Vahedi, Digestive Disease Research Center, Shariati Hospital, North Kargar Ave, Tehran 14117, Iran.
E-mail: vahedi@ams.ac.ir

*Publication data*
Submitted 28 April 2007
First decision 7 May 2007
Resubmitted 4 August 2007
Second decision 21 August 2007
Resubmitted 16 January 2008
Accepted 24 January 2008

## SUMMARY

### Background
Irritable bowel syndrome is the most common disorder diagnosed by gastroenterologists. Although several randomized-controlled trials have assessed the therapeutic role of antidepressant drugs, there is insufficient evidence to support their use.

### Aim
To compare the effects of low-dose amitriptyline in the treatment of diarrhoea-predominant irritable bowel syndrome in a double-blind randomized-controlled trial.

### Methods
Fifty-four patients who fulfilled Rome II criteria for diarrhoea-predominant irritable bowel syndrome were included in this study. Organic causes were ruled out by standard laboratory and radiological tests, and



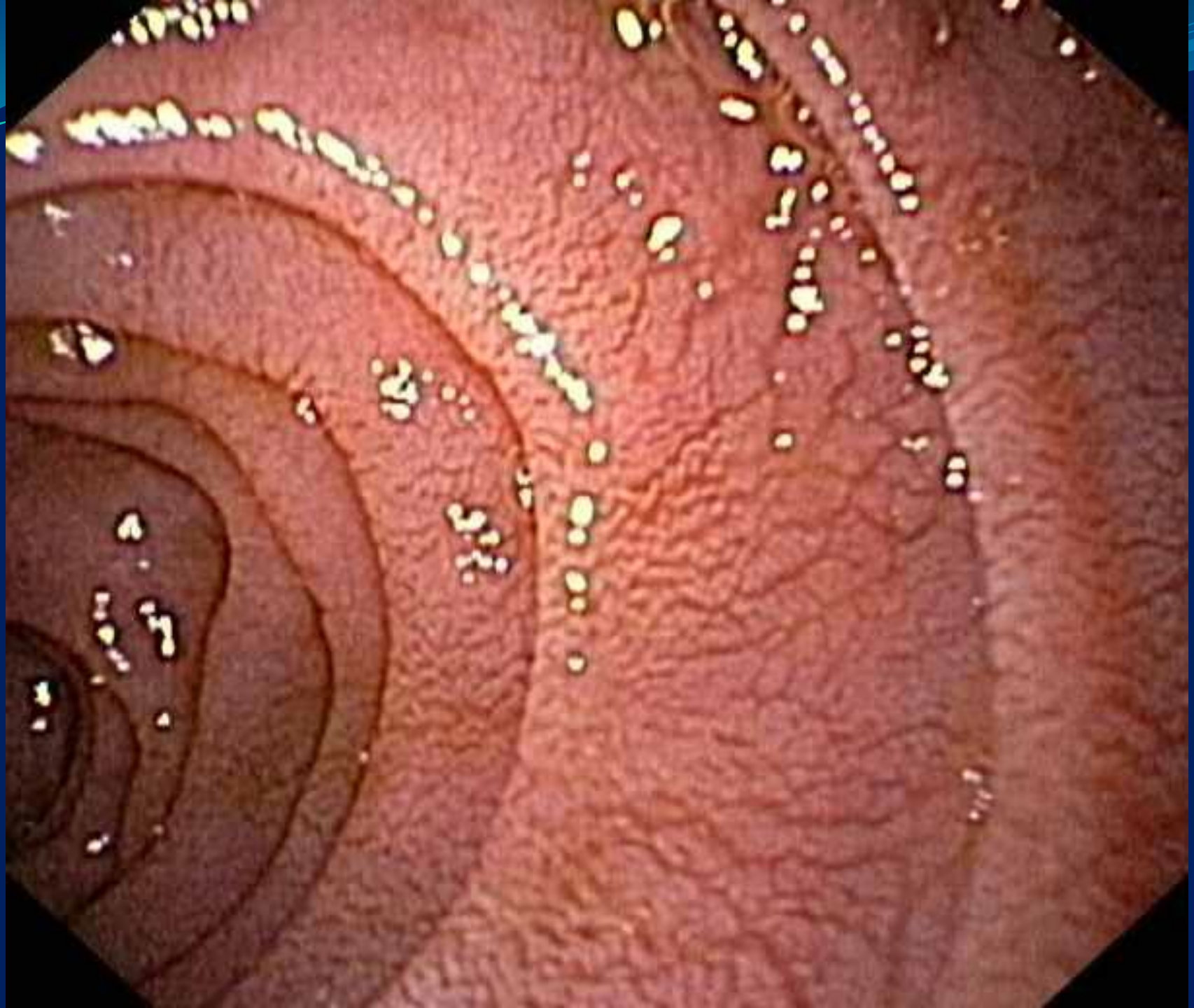
# Lab

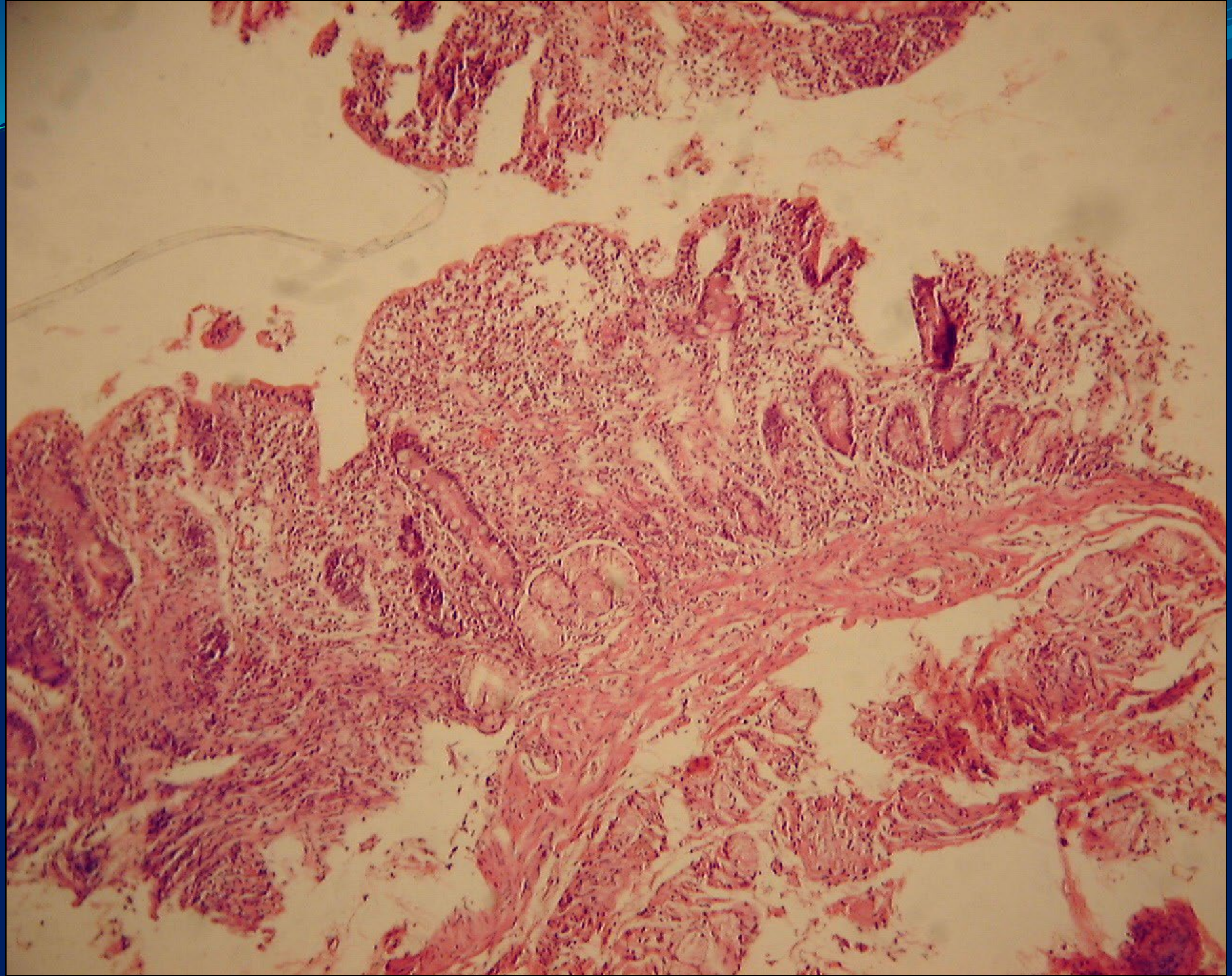
- Her Hb were always in the range of 10-11 and she was told to have an iron deficiency anemia and was treated with Fefol for last few years.
- Other Lab data were normal

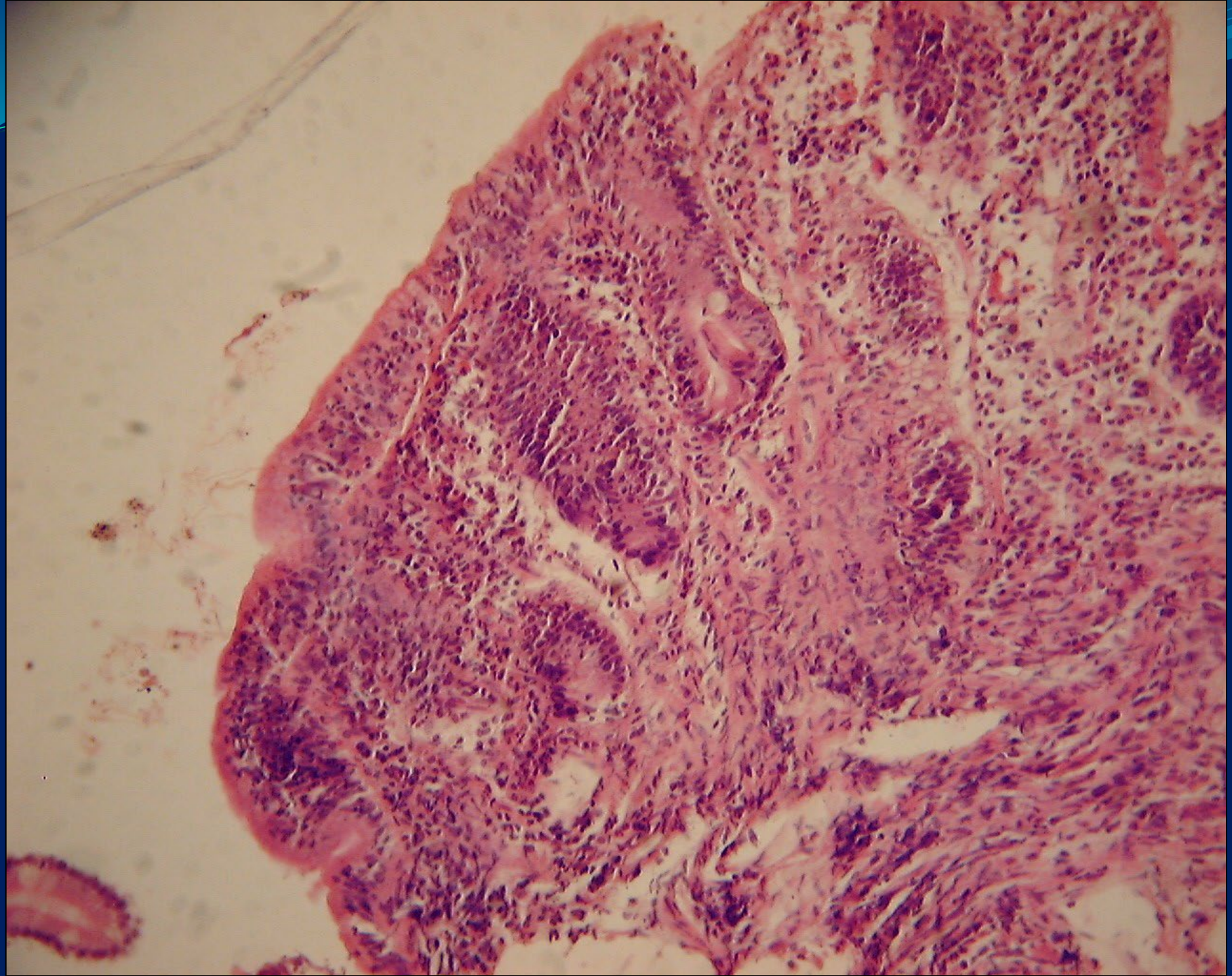
# Colonoscopy & Biopsy=Normal

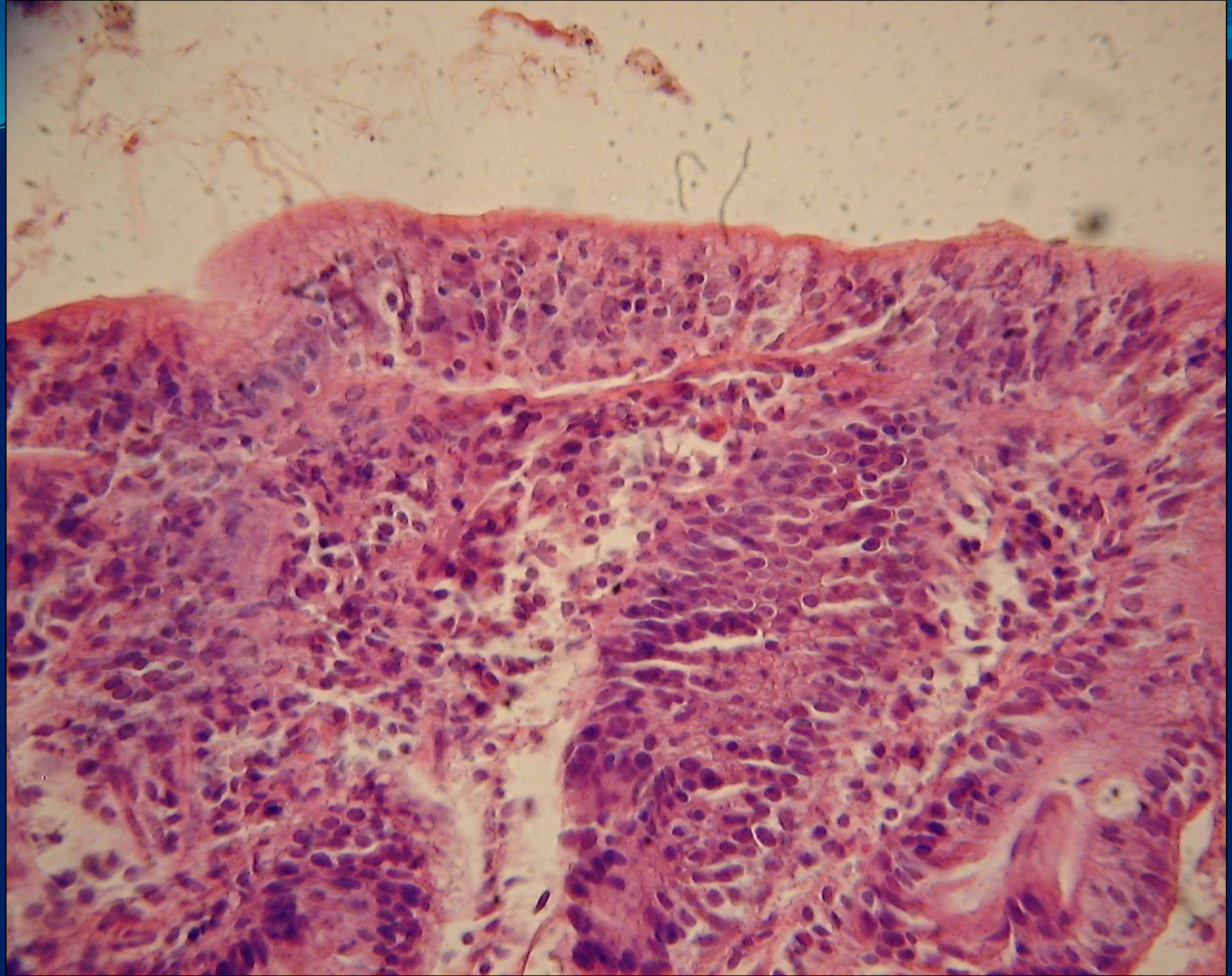


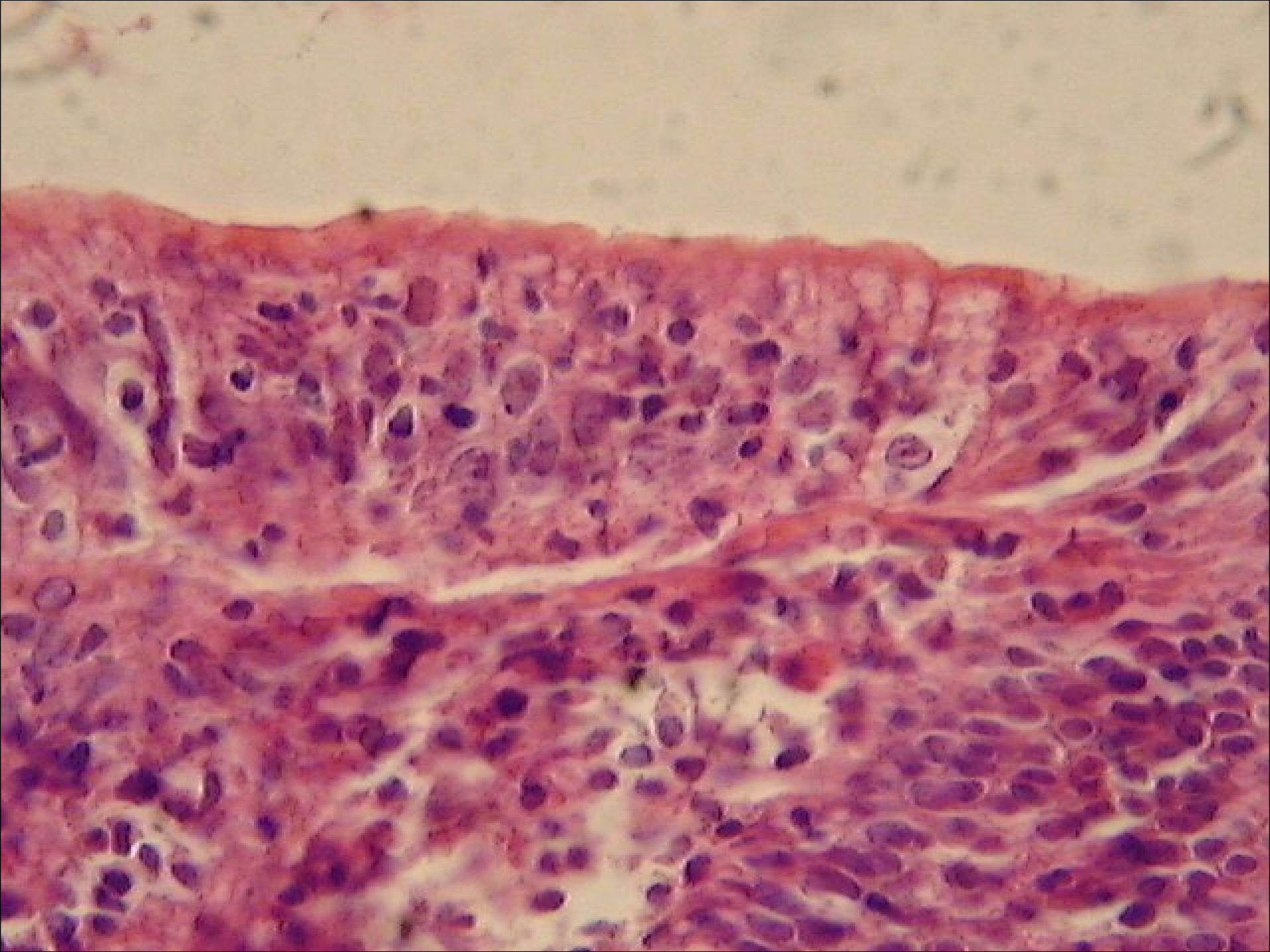






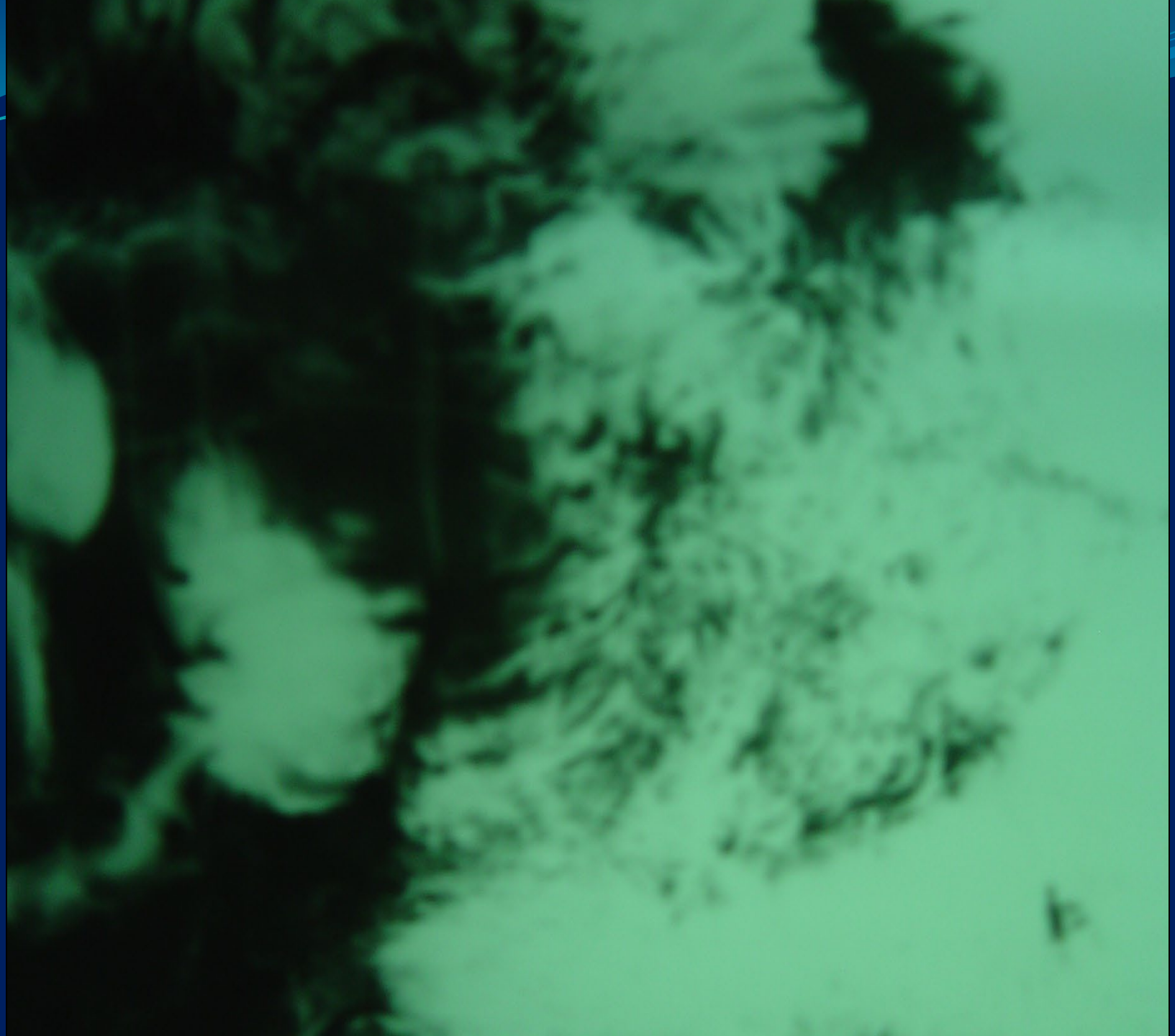


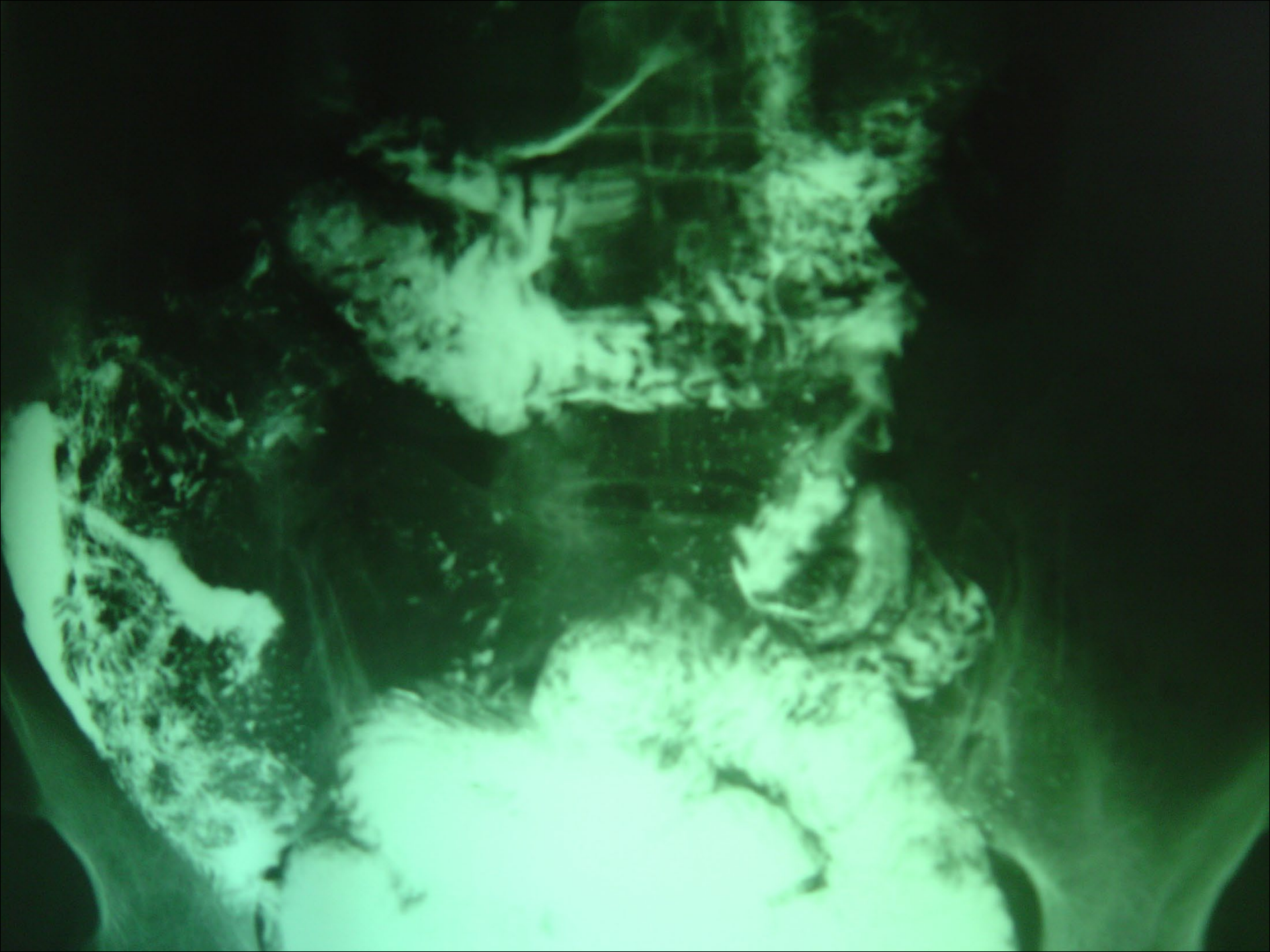


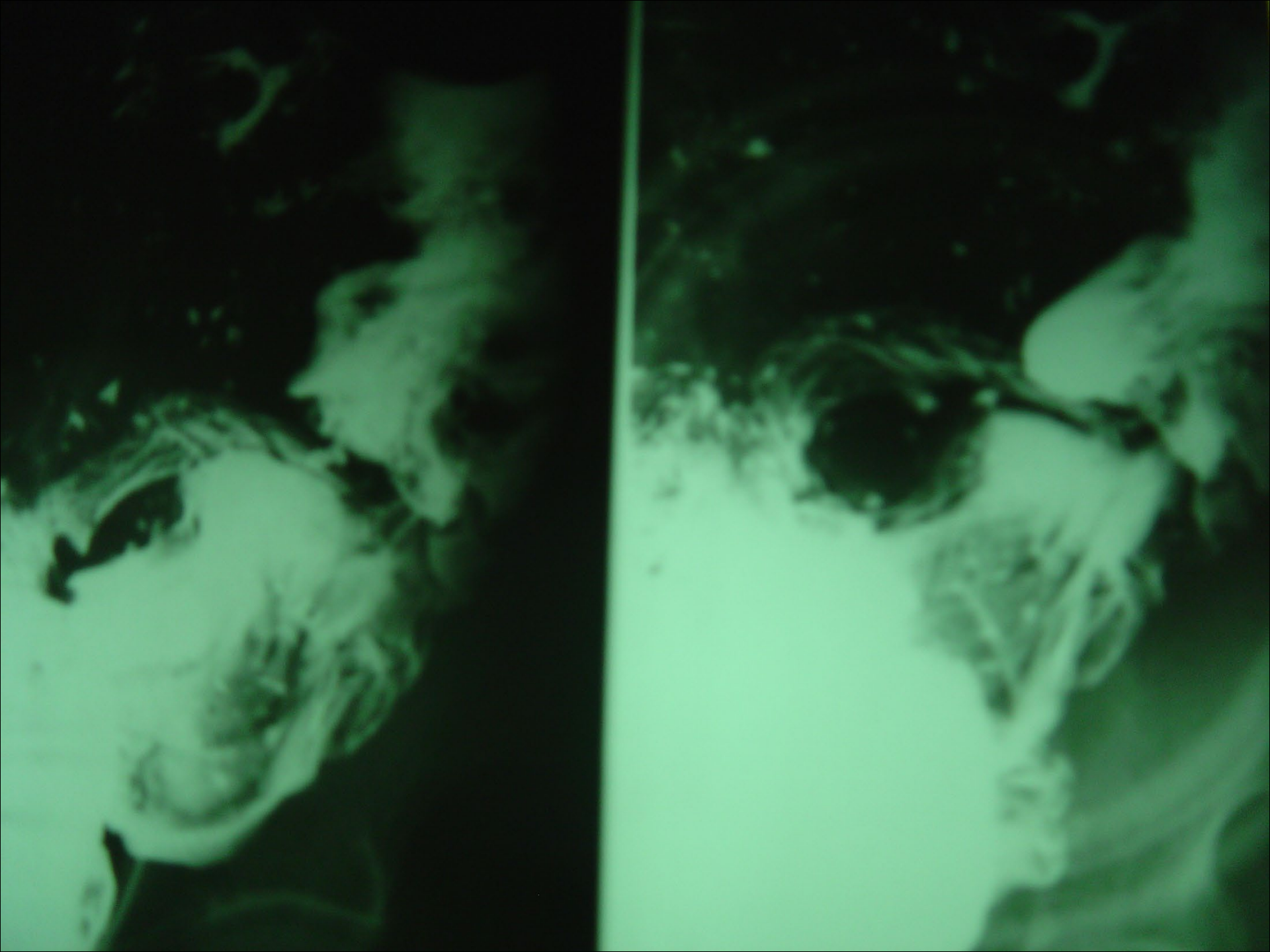


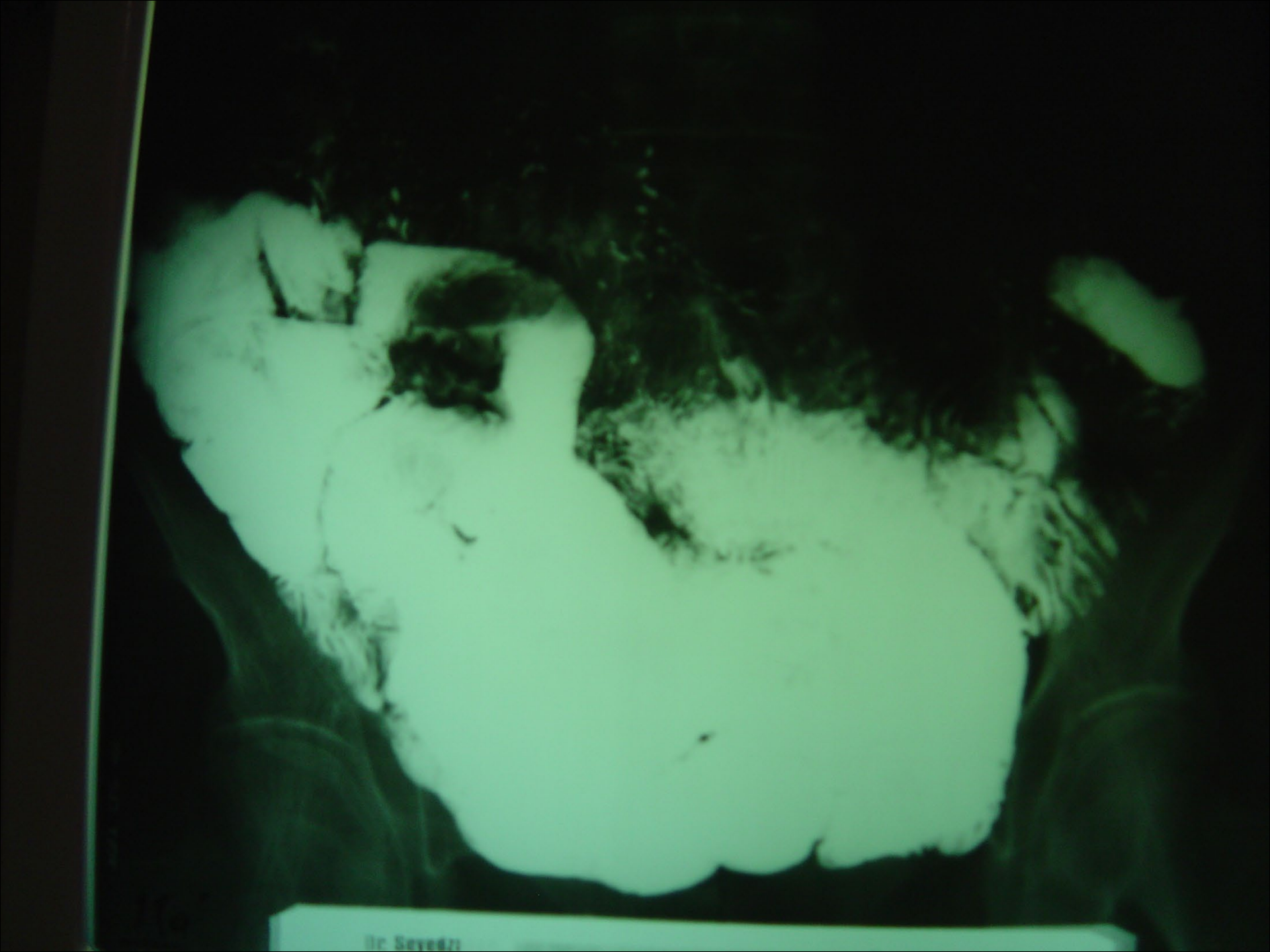
# Celiac Serology

- IgA-tTG=1/200 Positive
- IgA-EMA=1/100 Positive









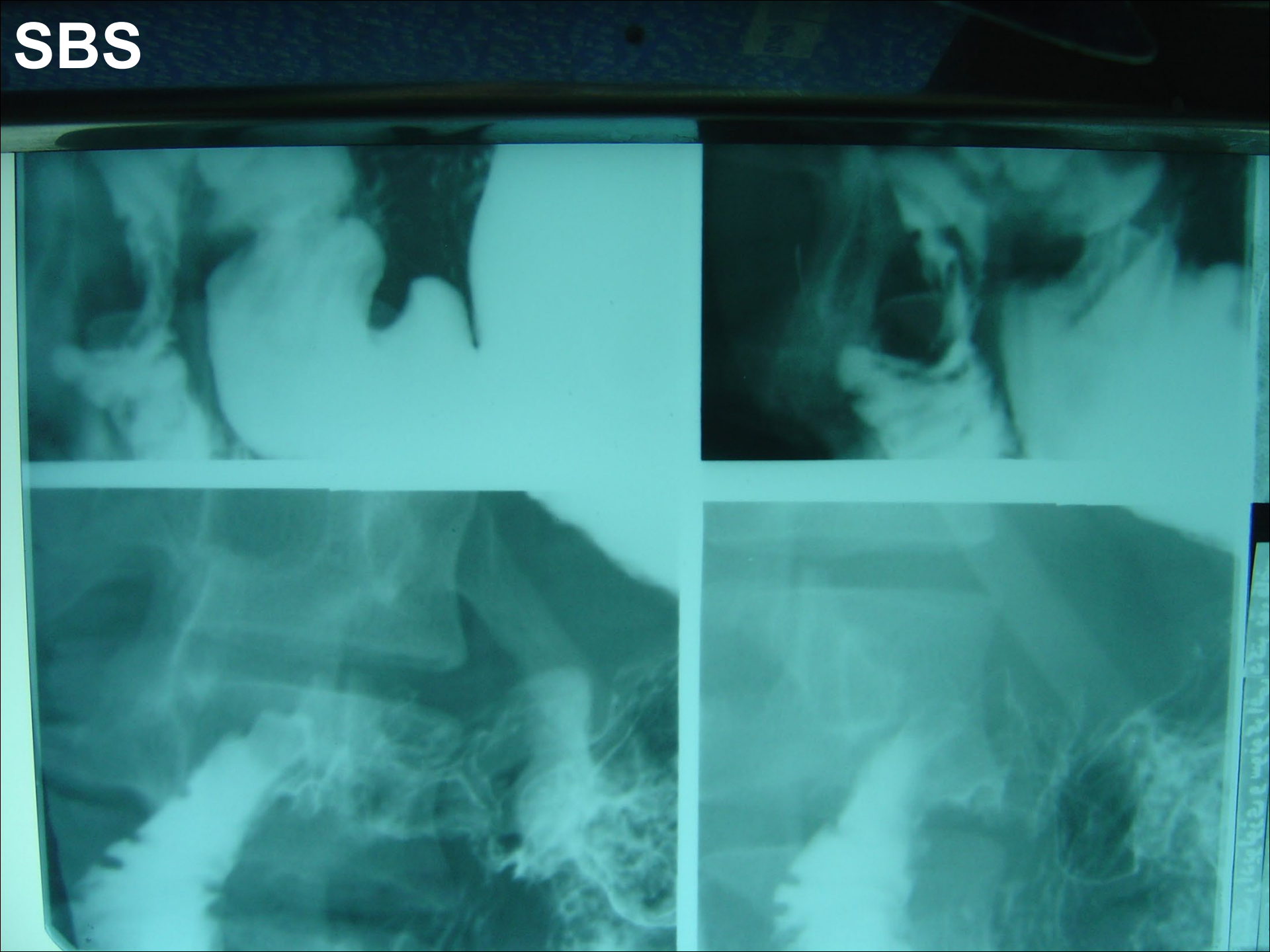
# Case 3

- 22 years old student presented with 7 months history of chronic  bloody mucus diarrhea, weight loss (6 kg) abdominal colicky RUQ and RLQ pain.
- PE =look wasted, tender RLQ area in abdomen.

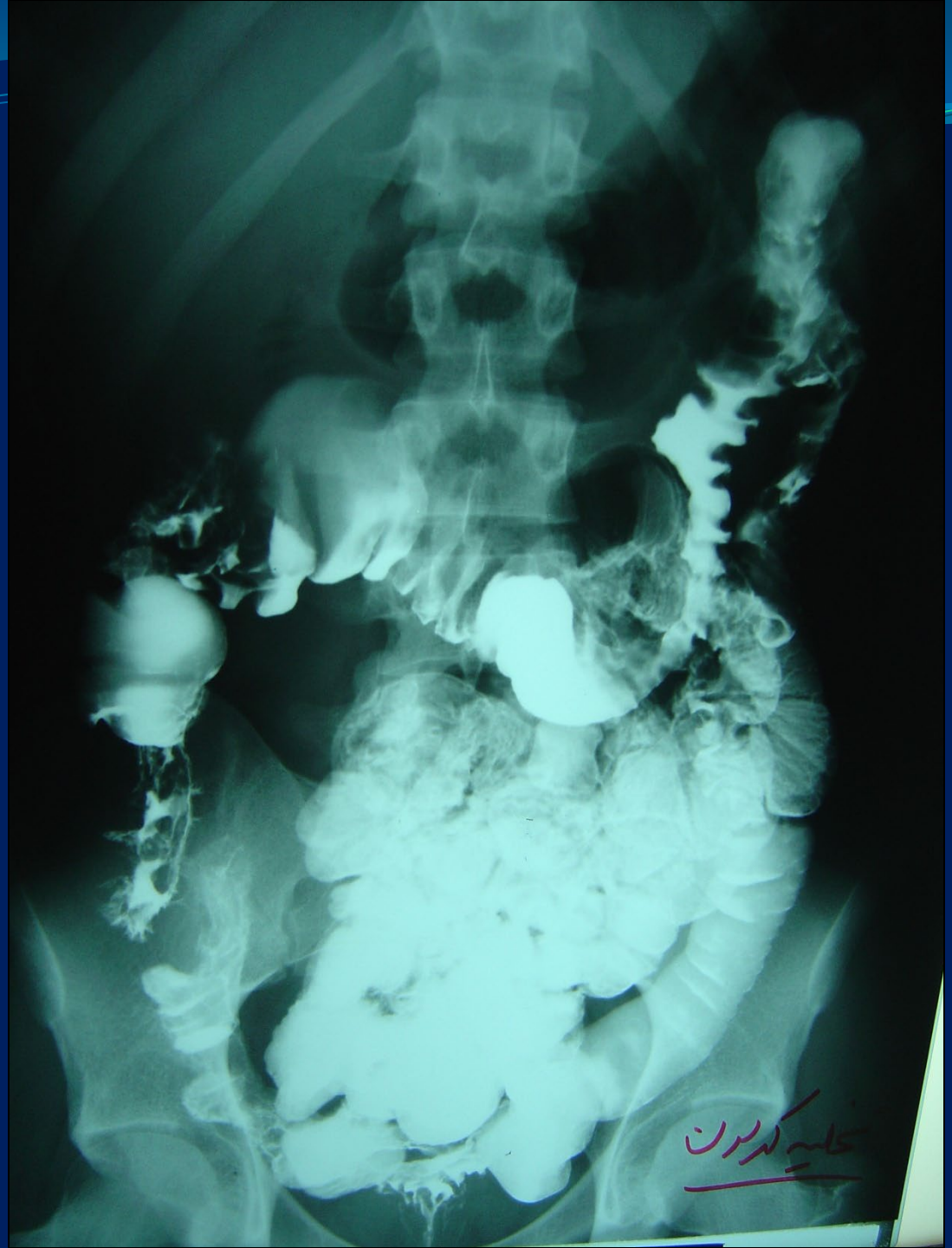
# LAB

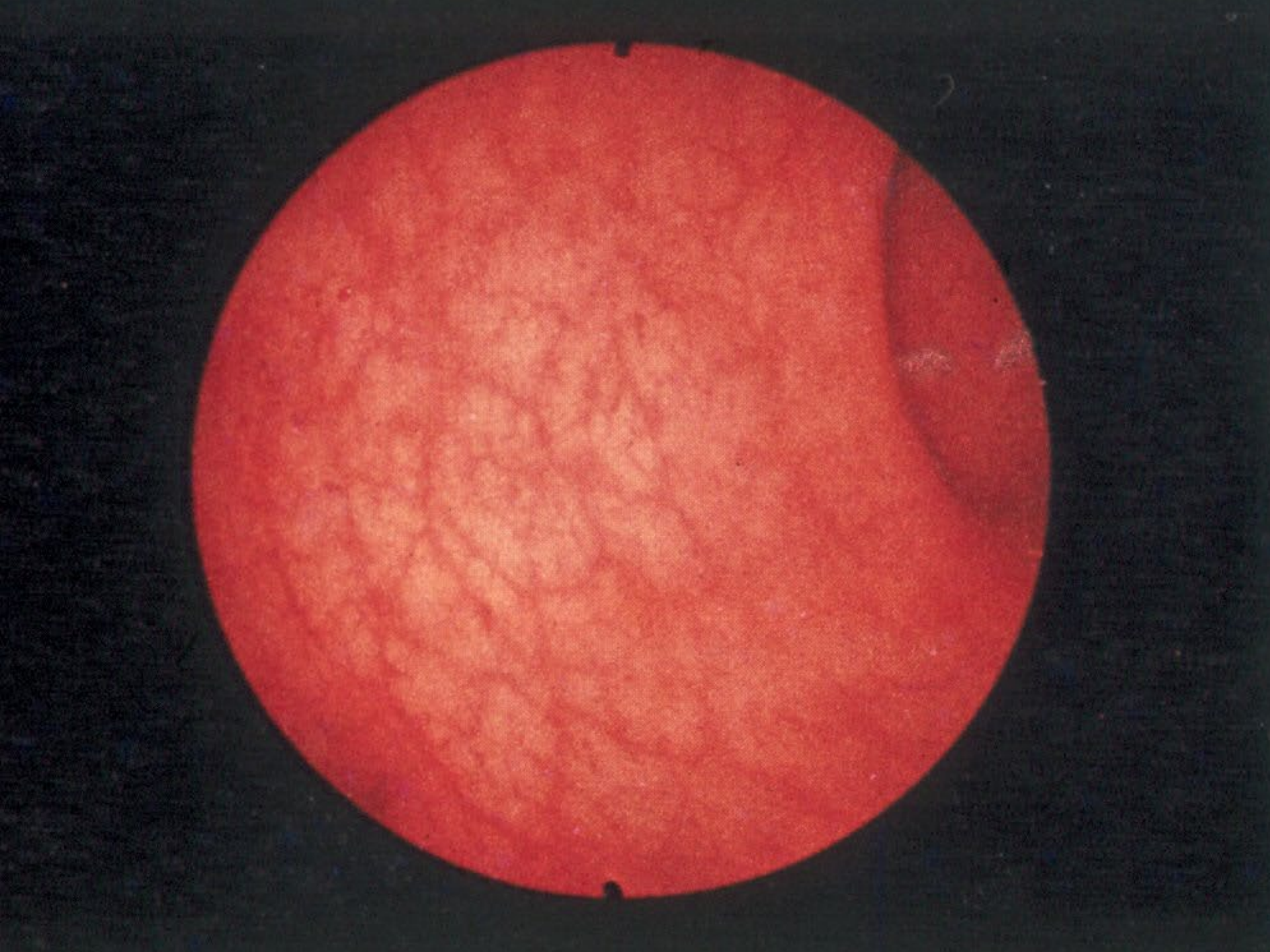
- Hb=10.5 MCV=74
- LFT=Normal
- Chemistry panel=nl.

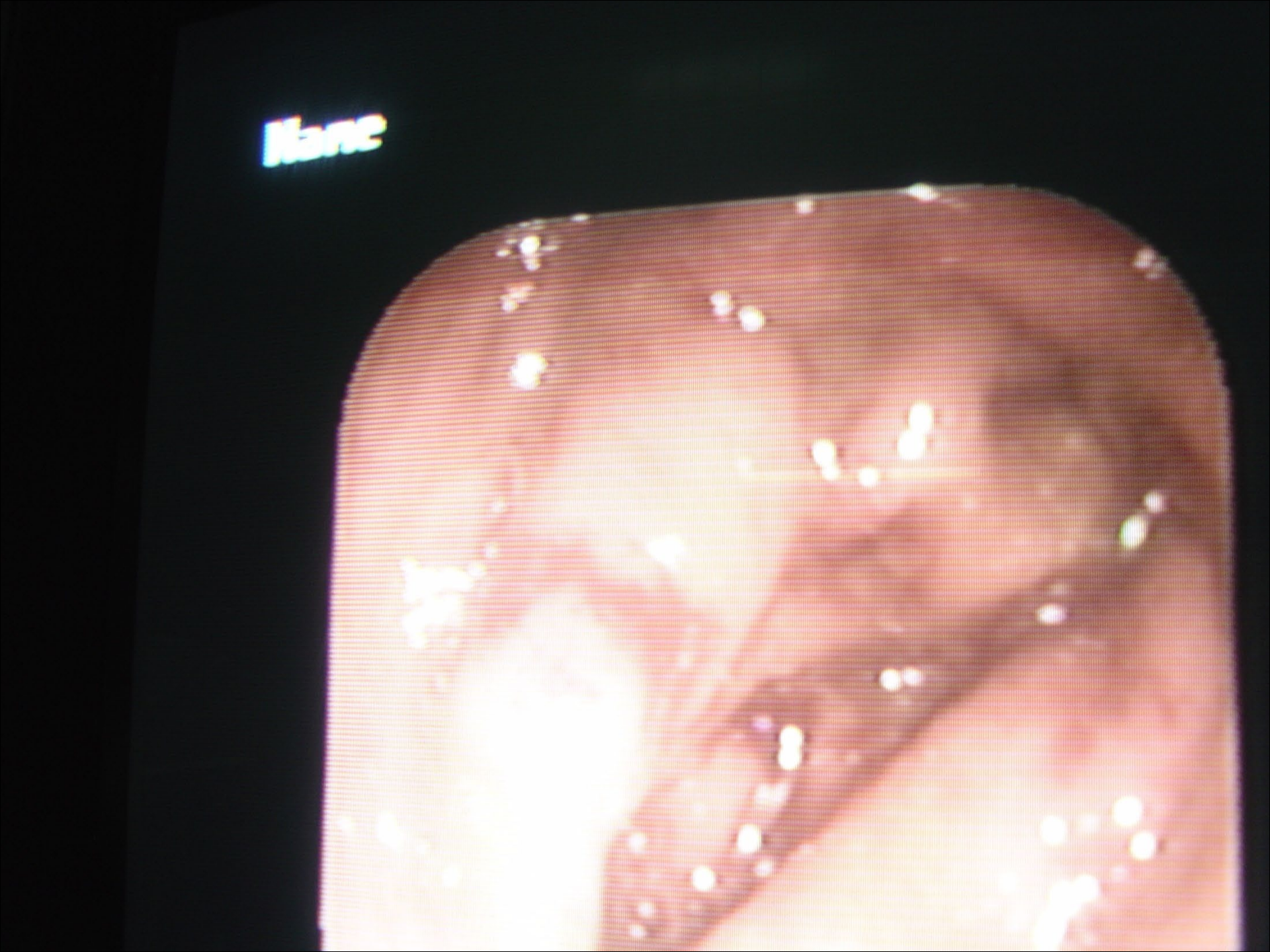
SBS

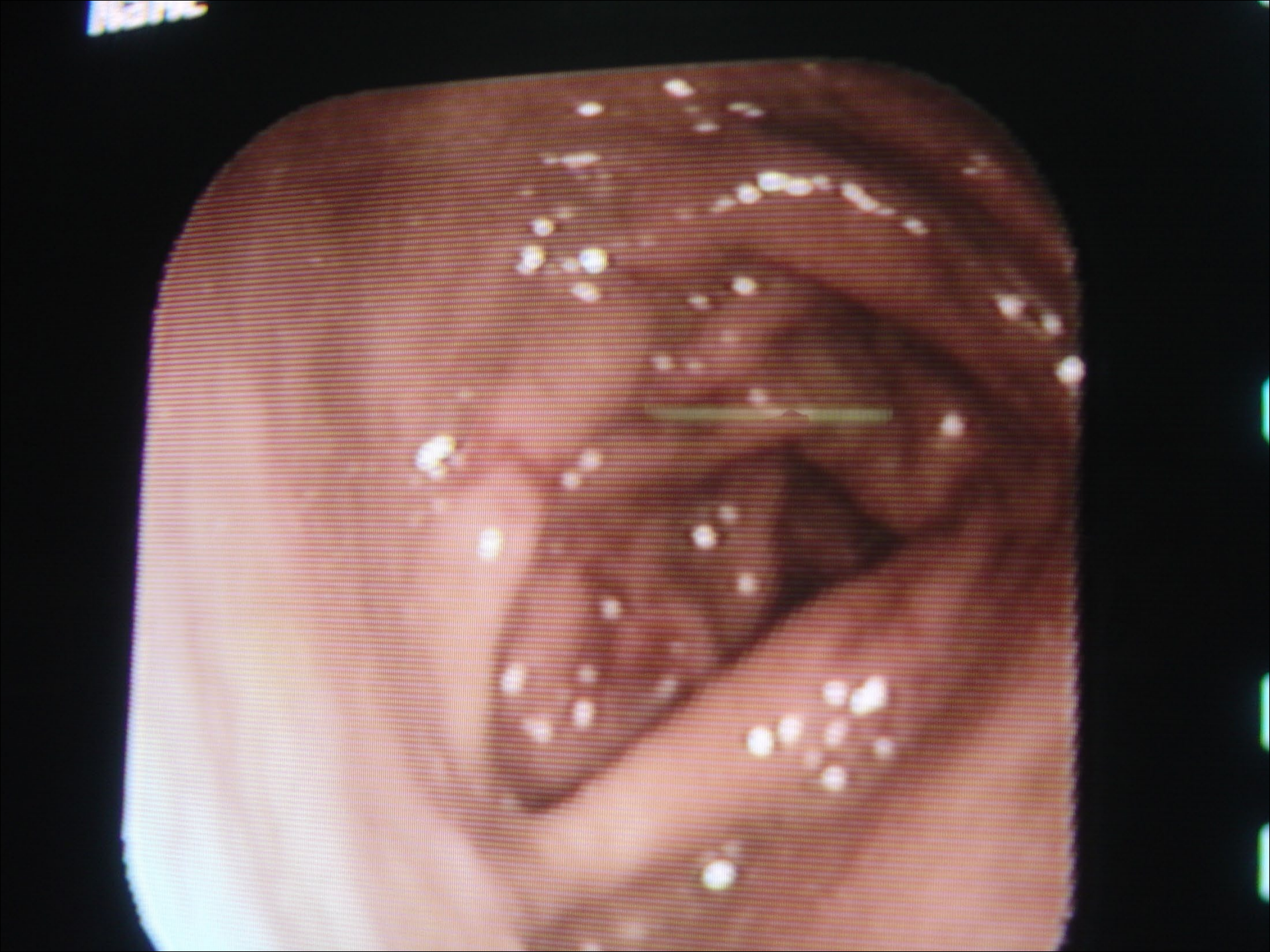


# DCBE











# Diagnosis

**DIAGNOSIS:**

**1- ASCENDING COLON, ULCERATIVE REGION, MUCOSAL BIOPSY:**
- CHRONIC CRYPT DESTRUCTIVE COLITIS, ACTIVE PHASE

**2- ASCENDING COLON, NORMAL REGION, MUCOSAL BIOPSY:**
- NO SIGNIFICANT PATHOLOGIC CHANGES

**3- TRANSVERSE COLON, MUCOSAL BIOPSY:**
- NO SIGNIFICANT PATHOLOGIC CHANGES

**4- SIGMOID COLON, MUCOSA BIOPSY:**
- NORMAL COLONIC MUCOSA EXCEPT FOR MILD GOBLET CELL DEPLETION

**5- RECTUM, MUCOSAL BIOPSY:**
- NORMAL COLONIC MUCOSA EXCEPT FOR MILD GOBLET CELL DEPLETION

**NOTE:**
Inflammatory bowel disease ( crohn's disease), prolonged enteric infection and drug
Clinico colonoscopic correlation are advised.

# Case 4

- A 52 years old housewife from Tehran Presented with watery diarrhea and 8 kg wt. loss of 4 months duration.
- There was no blood in stool .
- She also complain of episode of flushing and weakness.
- Physical Examination is normal except for wasting and apprehension,
- No mass no organomegaly.

# Case 3 Lab data

- Hb=13.5,WBC=5600,70% PMN
- BUN=23 Creatinine =1.1,Na=141,K=2.1
- Alk.phos=587,GGT=87,AST=27,ALT=19
- Abdominal Sonography & Ct scan of Abdomen revealed a 4x3 cm mass in the body of pancreas
- CT guided biopsy showed a well differentiated Iselt Cell tumor of Pancreas based on clinical finding most likely a Vipoma

# Case 6

37 Years old housewife with 3 years history of epigastric Pain and watery diarrhea and weight loss

. Physical Examination

was unremarkable except for 10kg wt. loss during last 3years

**Lab test** were normal except for

Hb=10.5 Mcv=76.

Her symptoms responded

partially to PPI

What is your next step?

# UGIE

- UGIE revealed GERD-B. Gastric ulcers an active bulbar duodenal ulcer with red spot,
- There was DAG with A positive Hp urease test.

❖ Which of the following is appropriate for This patient?

- 1-Endos.injection RX.with diluted EPN .
- 2-Hp eradication.
- 3-Biopsy of duodenum.
- 4-serum gastrin assay.

# Management

Injection of ulcer bed was performed by 12cc of :100 epin.

Omeprazole was given orally 40mg Q12hx2 da started.

She was discharged on the same day with AOFB x2w and omeprazole alone for 2 more weeks.

An appointment for UBT 3 months after the en was made.

# Follow up

- She came to clinic 3M later with a negative UBT.
- Her symptoms disappeared during therapy and 3w after the completion of therapy,
But reappeared again being milder than before
- But she still suffer by pain and pyrosis and diarrhea

# Lab Results

Fasting serum gastrin=928 pg/ml
Basal acid output=25meq/hr.
Secretin provocative test=+
SBS=unremarkable.

What is your next step(s) now?

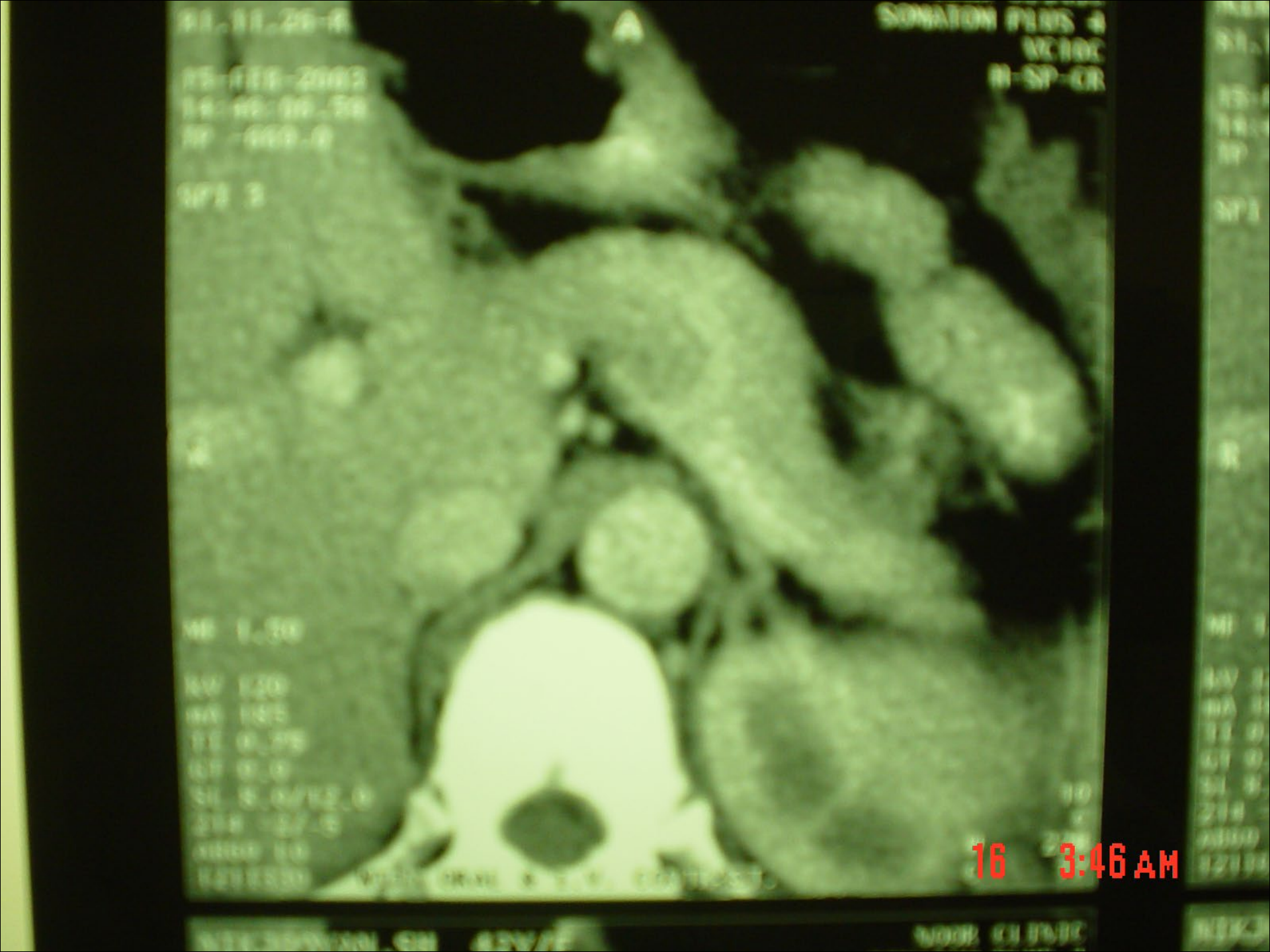
1-Life long PPI RX.

2-CT.,MRI,Angiography.

3-Somatostatin-receptor scintigraphy

4-Surgery.

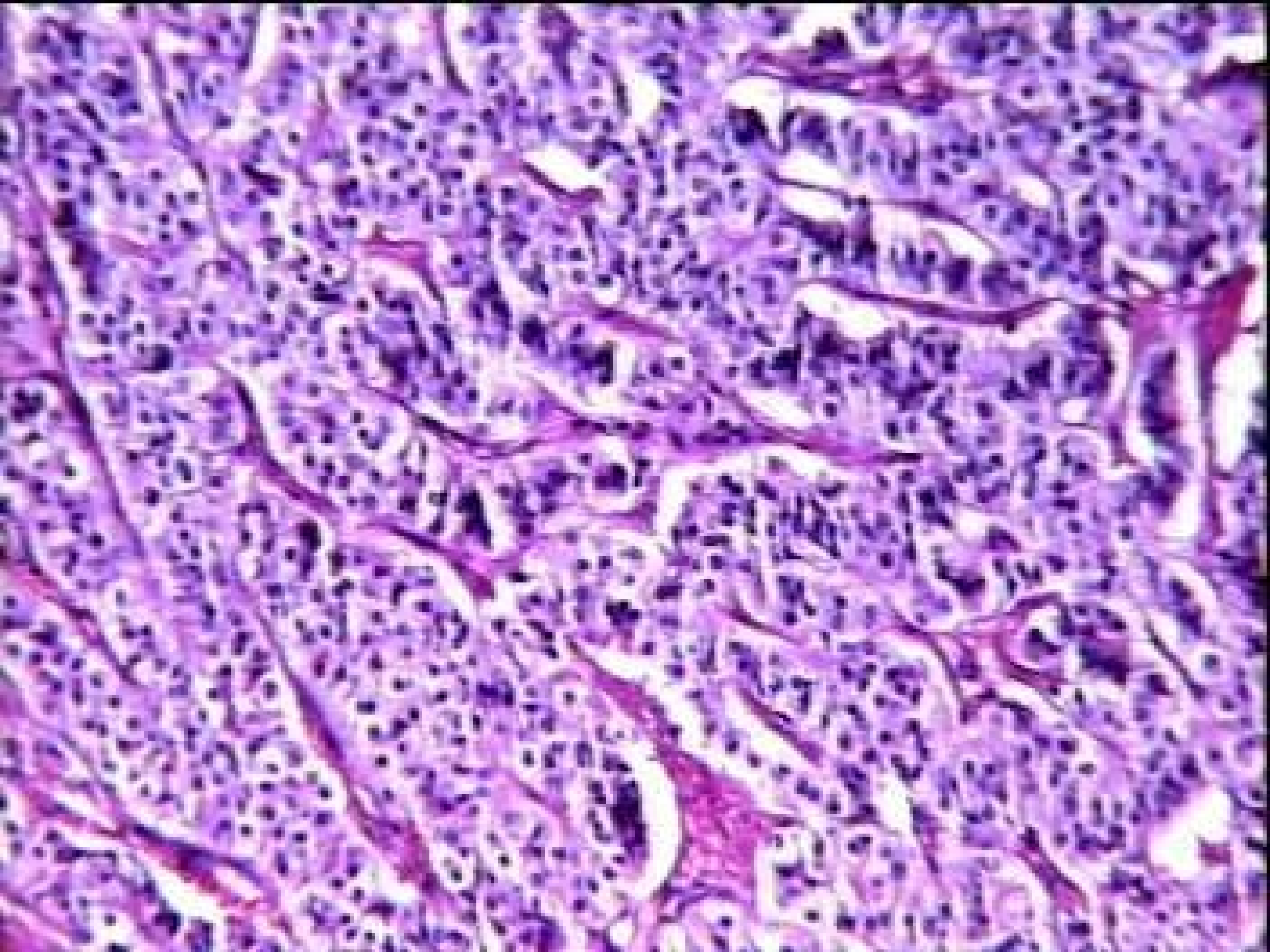

16 3:45 AM

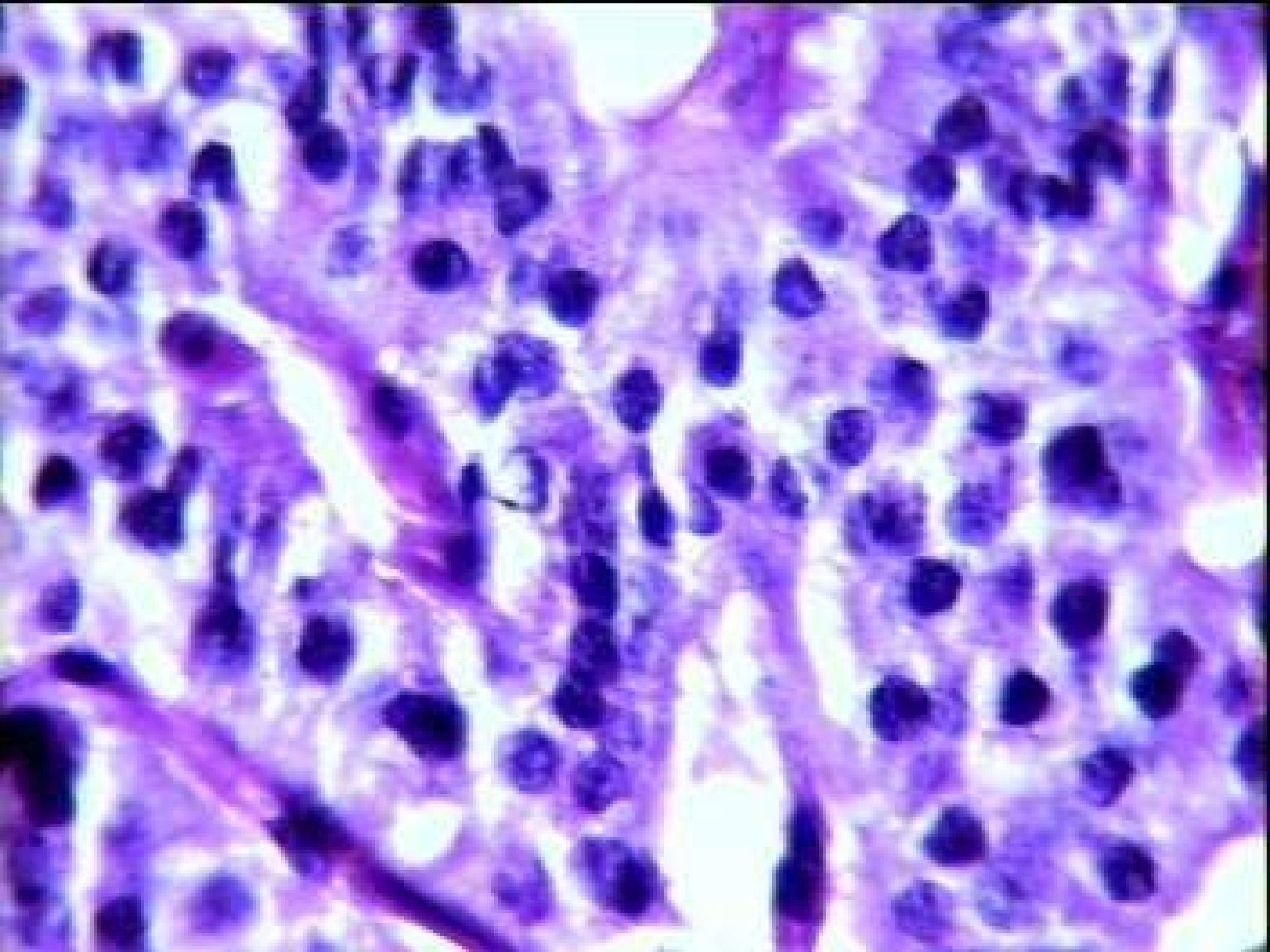

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# Follow up

- 2 months post op off omeprazole she remained asymptomatic 82/3/27
- FSG=38.5 micg/dl

# Follow up

- 82/5/14
- 5 months post op doing well asymptomatic

  no pain no diarrhea

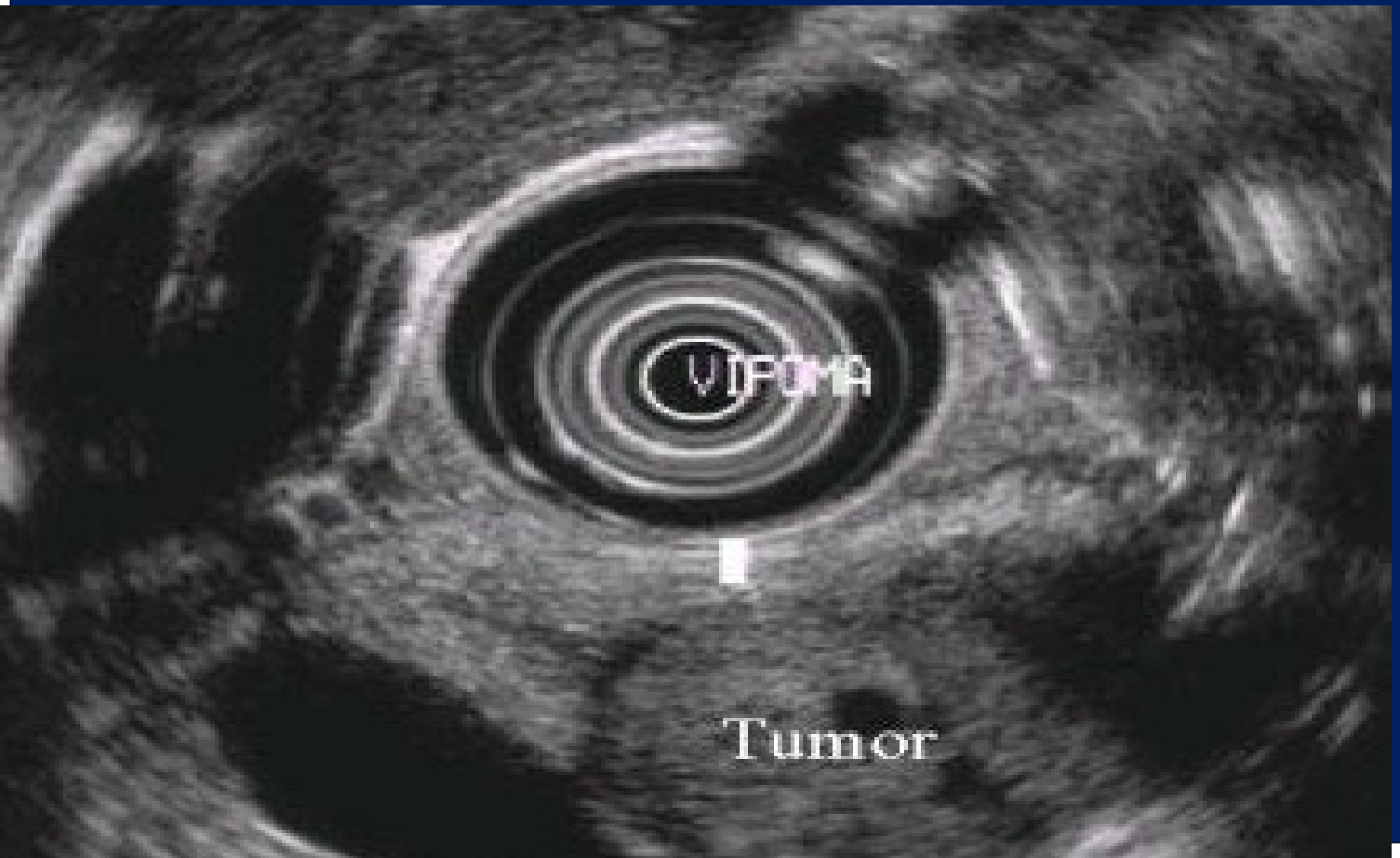
Fasting serum Gastrin=26.6 micg/dl

# Follow up Mehr 1384

## 4 year post op.

- Doing well asymptomatic
- FSG=36
- Normal Lab

# EUS finding



# What is your next step?

- Daily Octreotide subcutaneous injection .
- Surgery.
- Chemotherapy +Radiotherapy
- All of above

# FU

- Patient was started on Octreotide 50 microg subcutaneously every eight hours s and responded very well with disappearances of diarrhea and flushing.
- During operation 3 weeks later she was found to have an Islet cell tumor of pancreas with two small metastatic foci in the right liver lobe which were resected at the same time

## Post op.

- Post op she was doing well up to two years with occasional Octreotide injection for flushing.

She was missed for futher follow up when she moved to Shiraz.

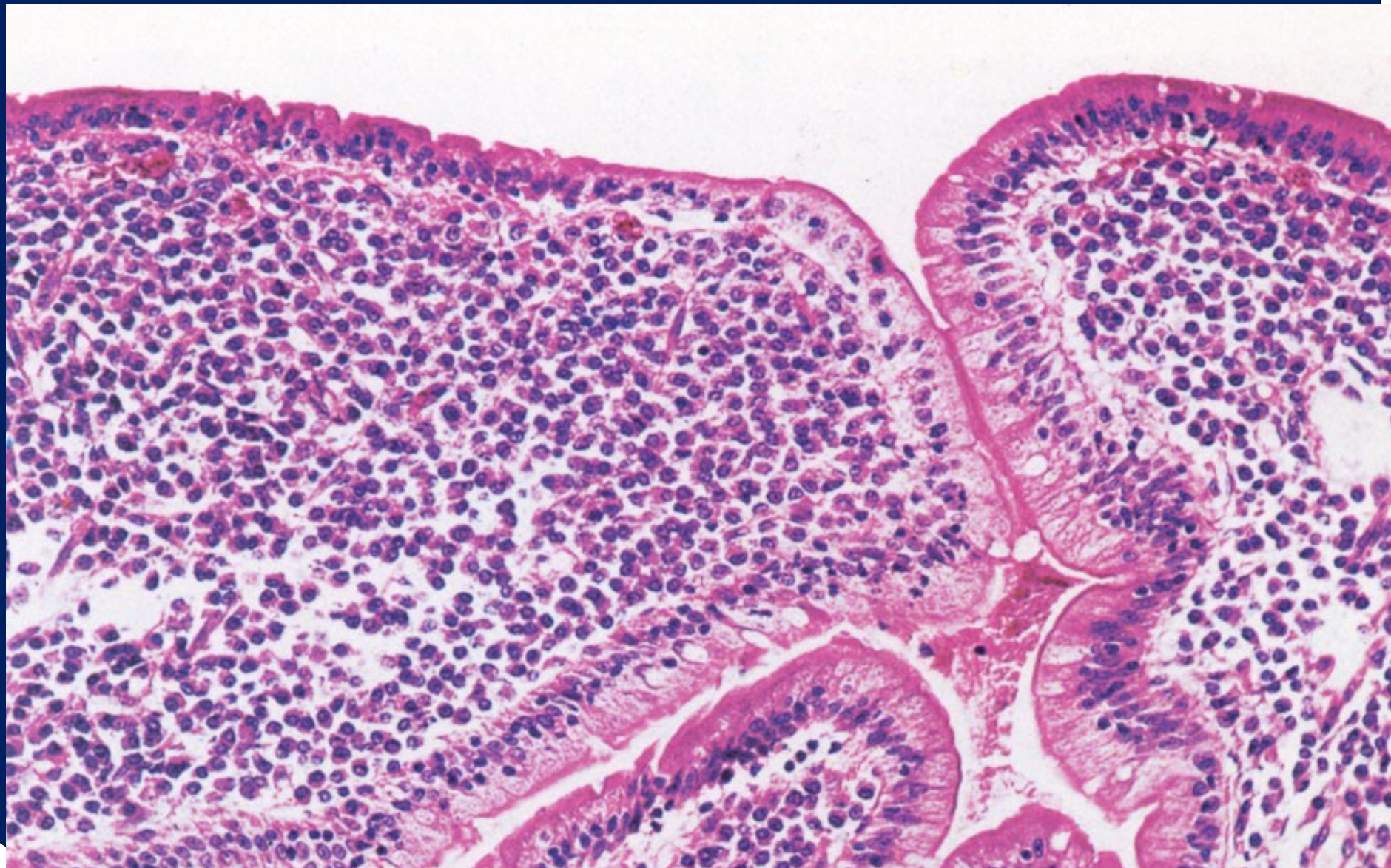
# Case 5: Shiraz 1364

- 28 years old housewife presented with 2 years history of voluminous diarrhea,12kg weight loss and pallor.
- She was found to have Hb=8.5 MCV=65
- 24 hour stool fat=12 gram

# Small bowel Series



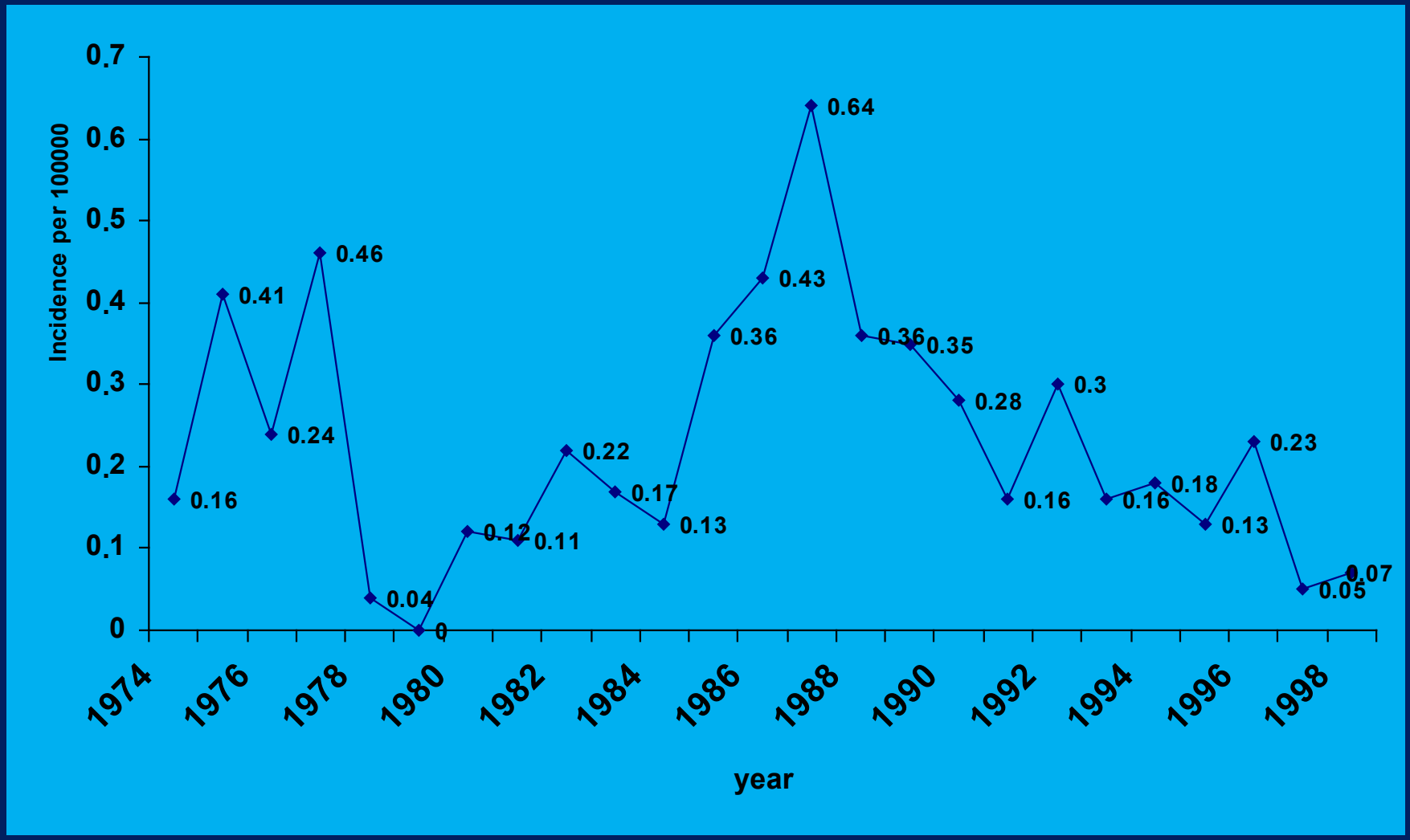
# Small Bowel Biopsy



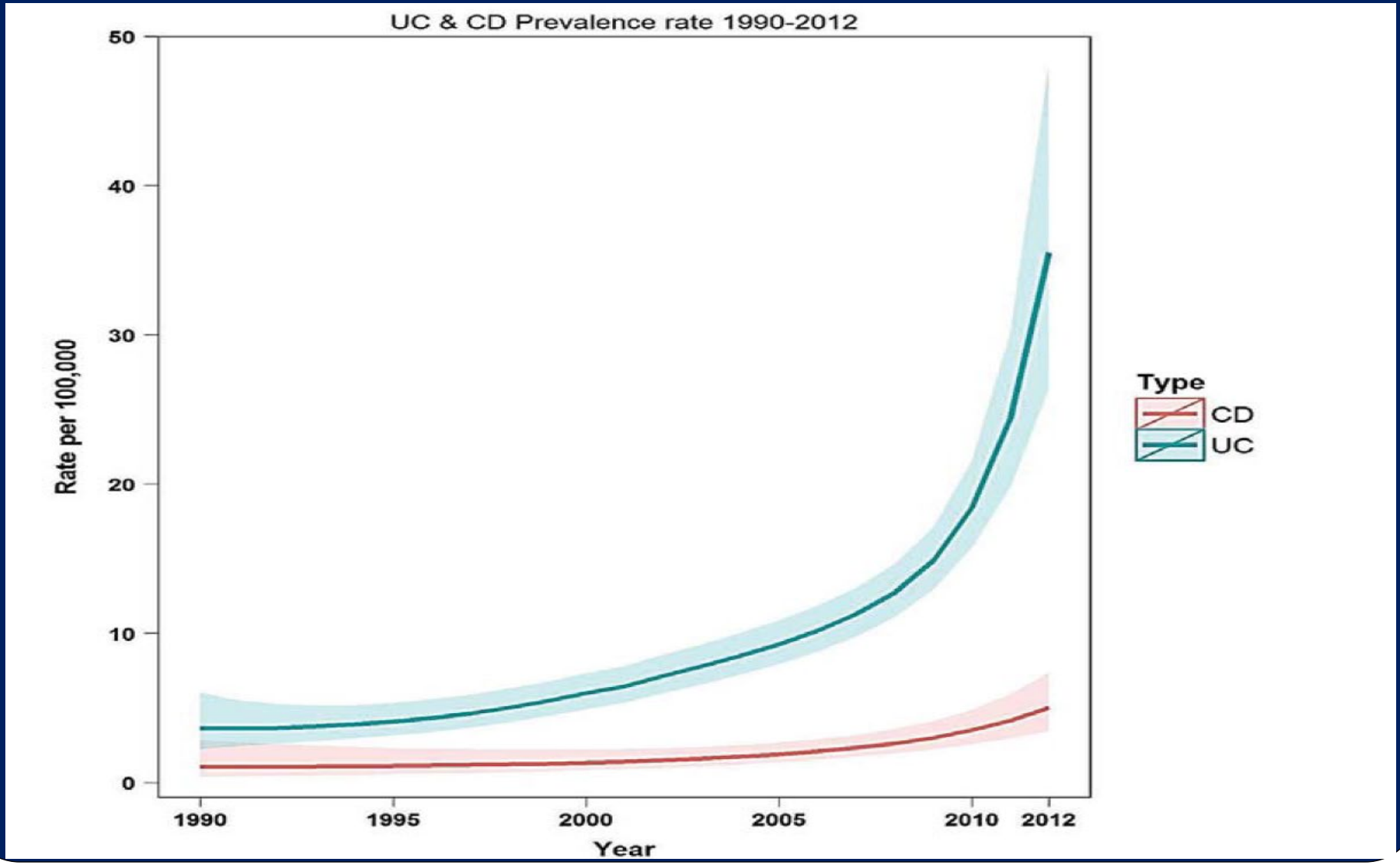
# IPSID

- Dense noninvasive monotypic plasma cell infiltrate in lamina propria
- Invasive infiltrate of centrocyte like cells in deeper layers
- Response to Antibiotics in their early stage
- Chemotherapy in advance state

# Incidence rate of IPSID from 1974 to 1998 in Fars province, Iran



# Prevalence UC and CD during 1990-2012 in Iran



# Increasing Incidence of Crohn's disease in Iran

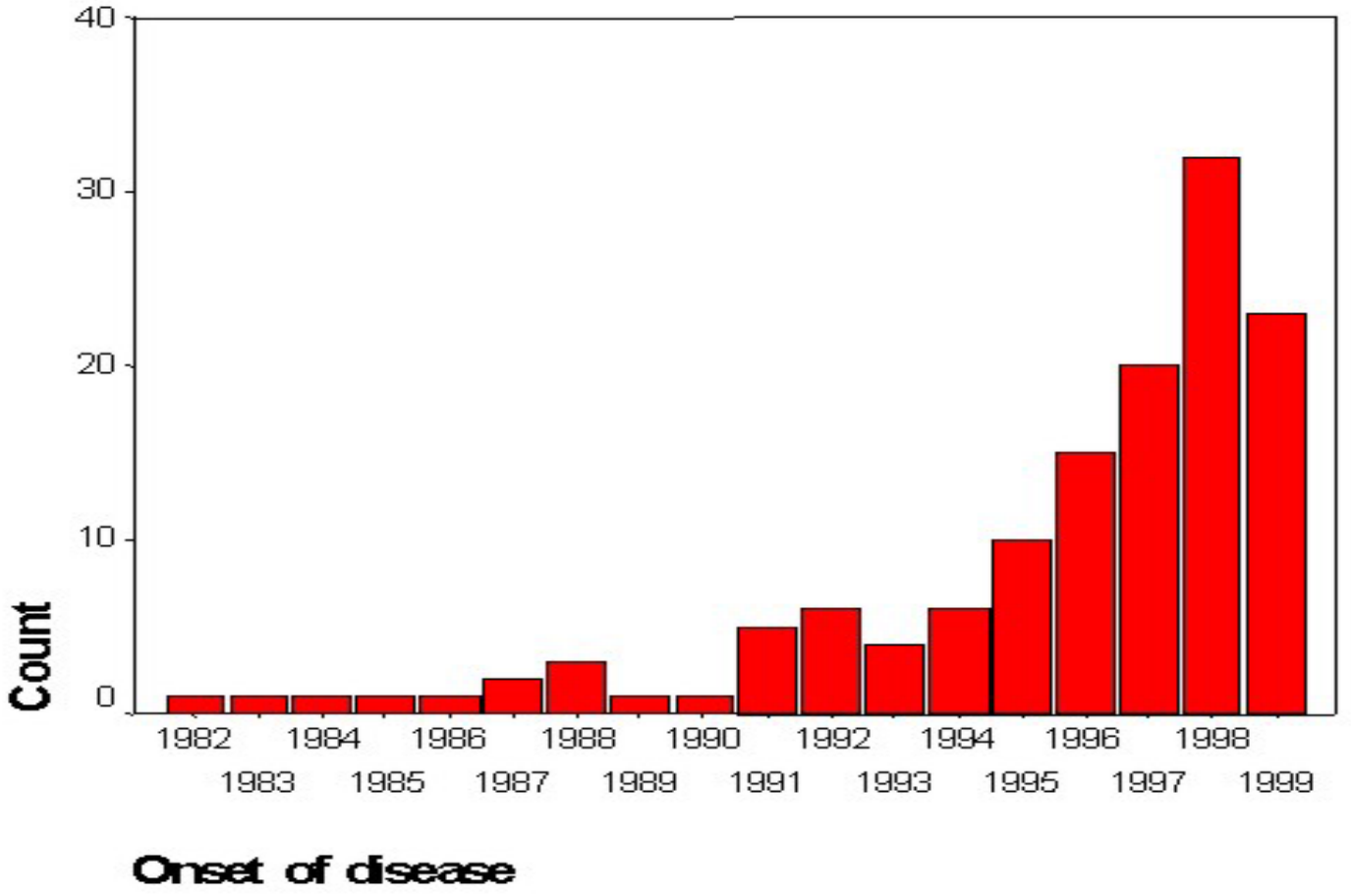



**Figure 2.** Increasing incidence of Crohn's disease

# Diarrhea specific death rate per 10000 among children aged < 5 yrs in Fars province 1989 to 1998

