Crohn's Disease

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Inflammatory bowel diseases

Definition

Inflammatory bowel diseases (IBDs), including ulcerative colitis and Crohn's disease, are chronic inflammatory diseases of the gastrointestinal tract. They are diagnosed by a set of clinical, endoscopic, and histologic characteristics.

Epidemiology-IBD

- The incidence is about 5 per 100,000.
- The prevalence is about 50 per 100,000.
- The peak age at onset
  - Between 15 and 25 years,
  - Second, lesser peak between 55 and 65 years.
- The incidence in children is low.
- The incidence is equal in men and women.
- Higher incidence in first-degree relatives
- The epidemiology varies with geographic location.

Pathogenesis

- Activated T cells are involved in the pathogenesis.
- Failure to suppress the normal, low-grade chronic inflammation of the intestinal lamina propria.
- Activated lymphocytes produce interferon-γ (IFN-γ).
- Pro-inflammatory cytokines, including interleukin-1 (IL-1) TNF-α, amplify the immune response.
- Epithelial injury in IBD appears to be due to reactive oxygen species from neutrophils and macrophages, as well as cytokines.

Pathology

- The bowel wall is thickened and stiff.
- The mesentery, which is thickened, edematous, and contracted, fixes the intestine in one position.
- Transmural inflammation may cause loops of intestine to be matted together.
- All intestinal layers are thickened,
- The intestinal lumen is narrowed.
- Colonic inflammation with rectal sparing is more consistent with Crohn's disease than with UC

Pathology-cont.

- Aphthous ulcers are the earliest lesions of CD.
- Aphthous ulcers → stellate or serpiginous → longitudinal and transverse linear ulcers.
- The remaining islands of nonulcerated mucosa give a cobblestone appearance.
- “Skip lesions” suggest Crohn's disease.
- Fissures develop from the base of ulcers and extend down through the muscularis to the serosa .
- Granulomas are common in Crohn's disease.

Clinical Manifestations

- Three major patterns:
  - (1) disease in the ileum and cecum (40 % of patients).
  - (2) disease confined to the small intestine (30 %).
  - (3) disease confined to the colon (25 %).
- Much less commonly, Crohn's disease involves more proximal parts of the gastrointestinal tract.
- The predominant symptoms are
  - Diarrhea.
  - Weight loss.
  - Abdominal pain.

Clinical Manifestations

- Patients may complain for months or years of vague abdominal pain and intermittent diarrhea.
- Diarrhea occurs in almost all patients.
- The pattern of diarrhea varies with the anatomic location:
  - Prolonged inflammation and scarring in the rectum may lead to incontinence
  - In disease confined to the small intestine, stools are of larger volume and not associated with urgency or tenesmus.
  - Patients with severe involvement of the terminal ileum and those who have undergone surgical resection of the terminal ileum may have bile salt diarrhea or steatorrhea.

Clinical Manifestations

- The location and pattern of pain correlate with location.
- Abdominal distention, nausea, and vomiting may accompany the pain.
- Weight loss of some degree occurs in most patients with Crohn's disease regardless of the anatomic location.
- Low-grade fever may be the first warning sign of a flare.
- Crohn's disease is a relapsing and remitting disease.

Clinical Manifestations

- **Physical findings**
- Physical findings in Crohn's disease vary with the distribution and severity of the disease.
- Aphthous ulcers of the lips or buccal mucosa are common.
- The abdomen may be tender.
- Thickened bowel loops, thickened mesentery, or an abscess may cause a mass,
- Perianal disease is suggested by fistulous openings, induration, redness, or tenderness near the anus

Clinical Manifestations

- **Laboratory findings**
- largely nonspecific.
- Anemia may result from
  - Chronic disease, or Blood loss.
  - Nutritional deficiencies.
- Elevated leukocyte count ;
  - Modest elevation is indicative of active disease.
  - Marked elevation is suggestive of suppurative complication.
- ESR has been used to monitor disease activity.
- Hypoalbuminemia is an indication of malnutrition.
- Ileal disease or resection may result in malabsorption.

Clinical Manifestations

CRITERIA FOR SEVERITY IN IBD	
Mild	Fewer than 4 bowel movements per day with little or no blood, no fever, and sedimentation rate less than 20 mm/h.
Moderate	Between mild and severe.
Severe	Six or more bowel movements per day with blood, fever, anemia, and sedimentation rate greater than 30 mm/h.

Extraintestinal Manifestations of IBD

The extraintestinal manifestations can be divided into two major groups:

- (1) those in which the clinical activity follows the activity of the bowel disease and
- (2) those in which the clinical activity is unrelated to the activity of the bowel disease.

Extraintestinal Manifestations of IBD

- **Arthritis**

  Most common extraintestinal manifestation of IBD

- Colitic arthritis
  - Migratory arthritis
  - Parallels the course of the bowel disease
  - Affects the knees, hips, ankles, wrists, and elbows.
- Ankylosing spondylitis
  - Characterized by morning stiffness and low back pain
  - 30-fold increase in the incidence in patients with UC.
  - Treatment of the IBD are not helpful in managing ankylosing spondylitis.

Extraintestinal Manifestations of IBD

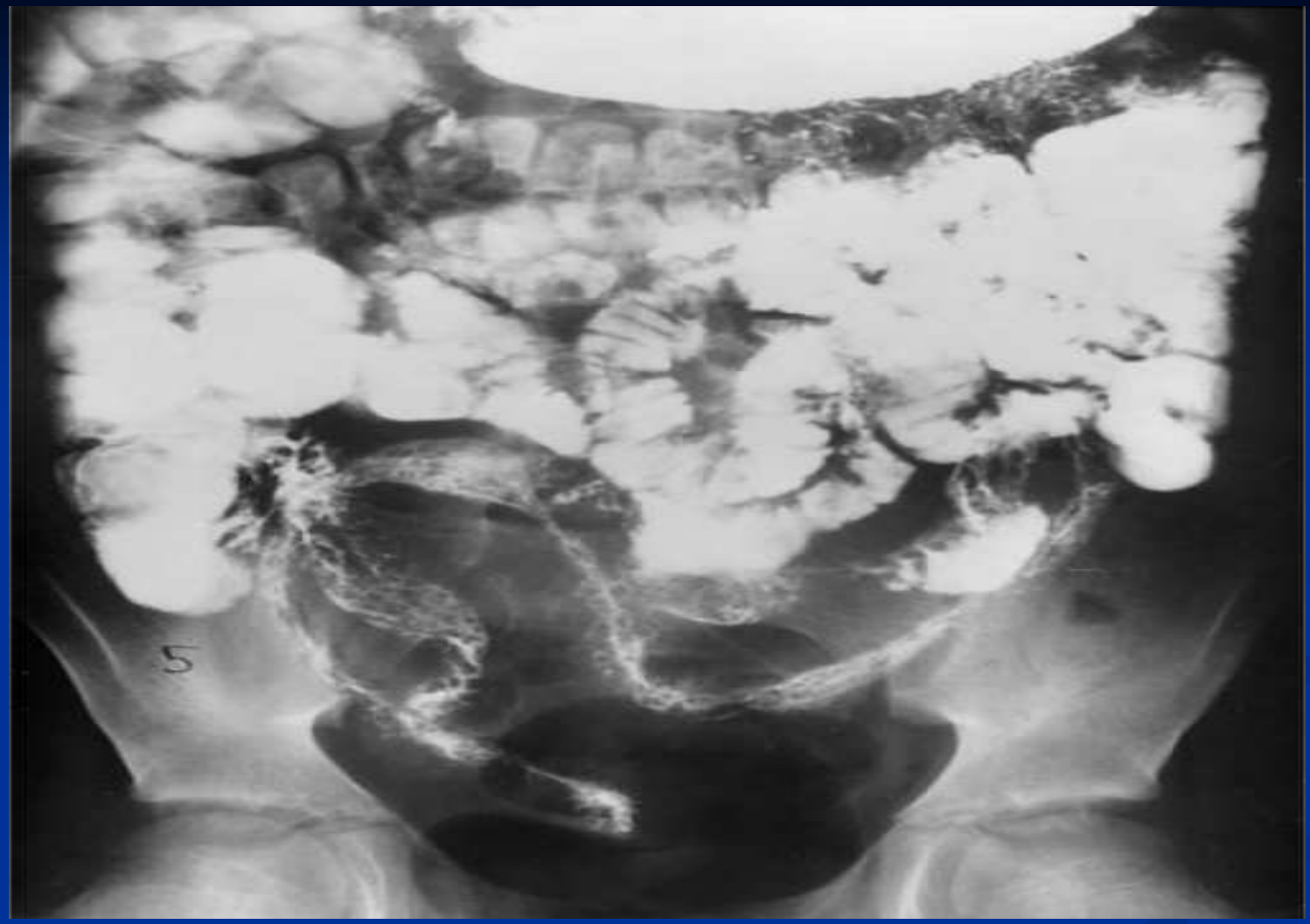
- **Hepatic complications**
  - Fatty liver, chronic active hepatitis, and cirrhosis.
  - Pericholangitis is the most common hepatic complication.
- **Biliary tract complications**
  - Sclerosing cholangitis (UC).
  - Gallstones (Crohn's disease).
- **Sclerosing cholangitis**
  - Occurs in 1 to 4% of patients with UC
  - lower frequency in Crohn's disease.
  - Treatment of IBD doesn't ameliorate the course.

Extraintestinal Manifestations of IBD

- **Dermal manifestations**
- Pyoderma gangrenosum
  - Usually develop during a bout of acute colitis
  - Resolve with control of the colitis.
  - In rare cases, colectomy is required.
- The activity of erythema nodosum,
  - Seen in association with Crohn's disease in children,
  - Follows the activity of the bowel disease.
- **Ocular manifestations**
  - Ocular complications of IBD are uveitis and episcleritis.

Diagnosis

- **Radiography**
- Contrast studies/ air contrast barium enema may show
  - Presence of aphthous ulcers.
  - Nodular appearance on radiographs.
  - Presence of fistulas.
  - Thickening of the bowel wall.
  - Decreased luminal diameter and stricture formation.
  - Small bowel can be evaluated by bowel follow-through.
  - CT and US are useful in identifying abscesses, fluid collections and bowel wall thickness.

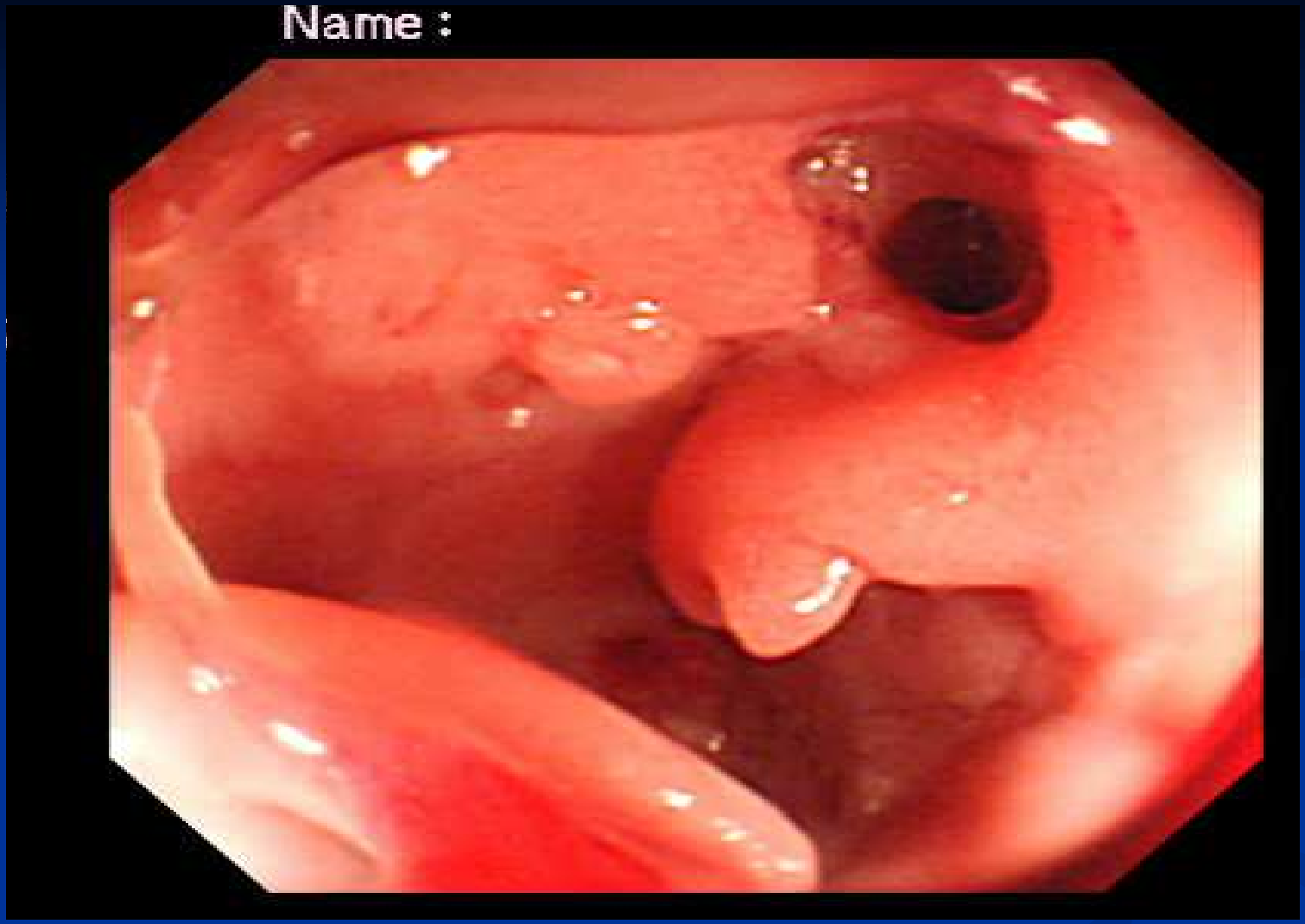


Small bowel follow-through in a patient with Crohn's disease of the ileum. Luminal narrowing, mucosal ulceration, and separation of the barium-filled loops because of thickening of the bowel wall

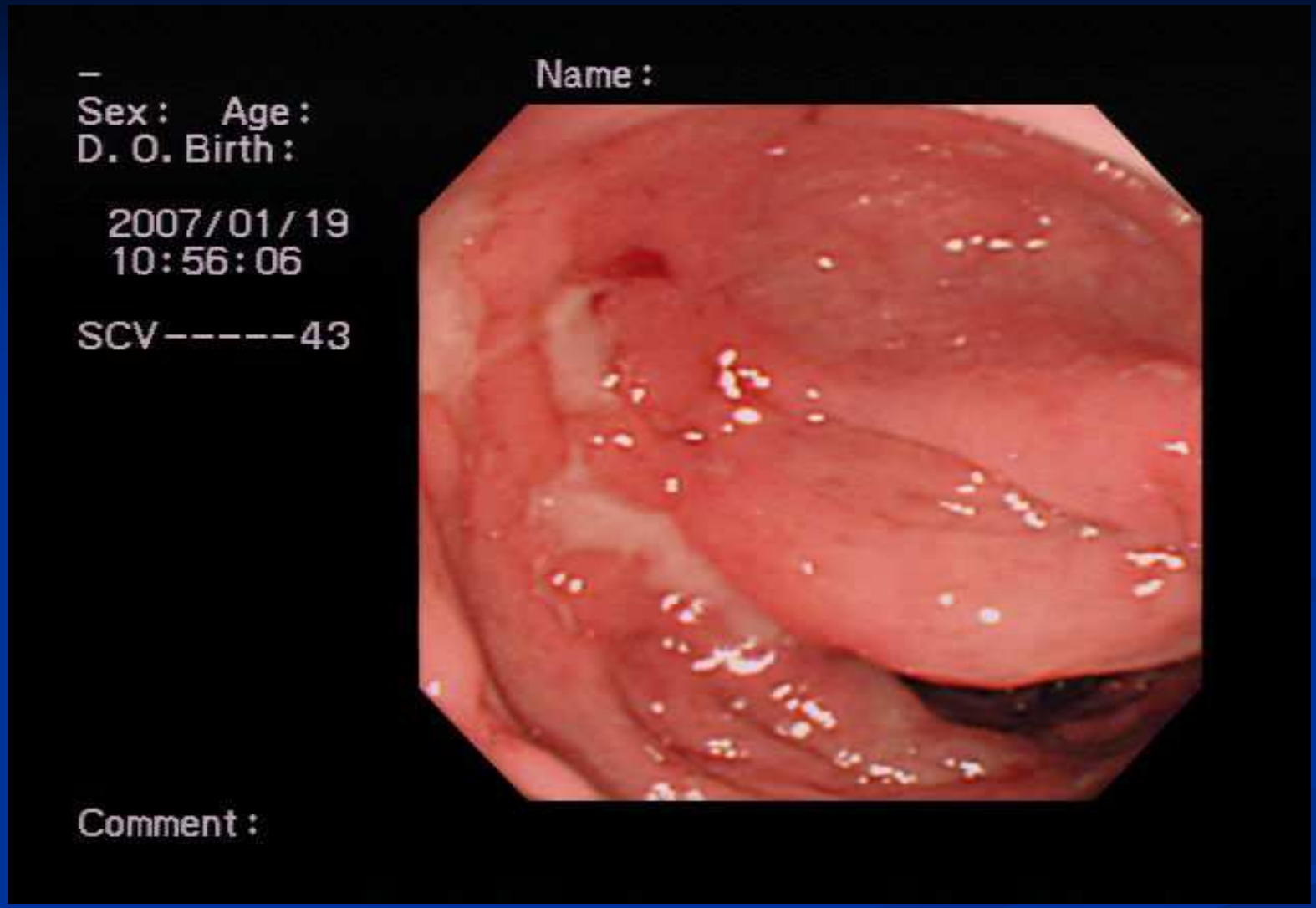
Diagnosis

Endoscopic features include

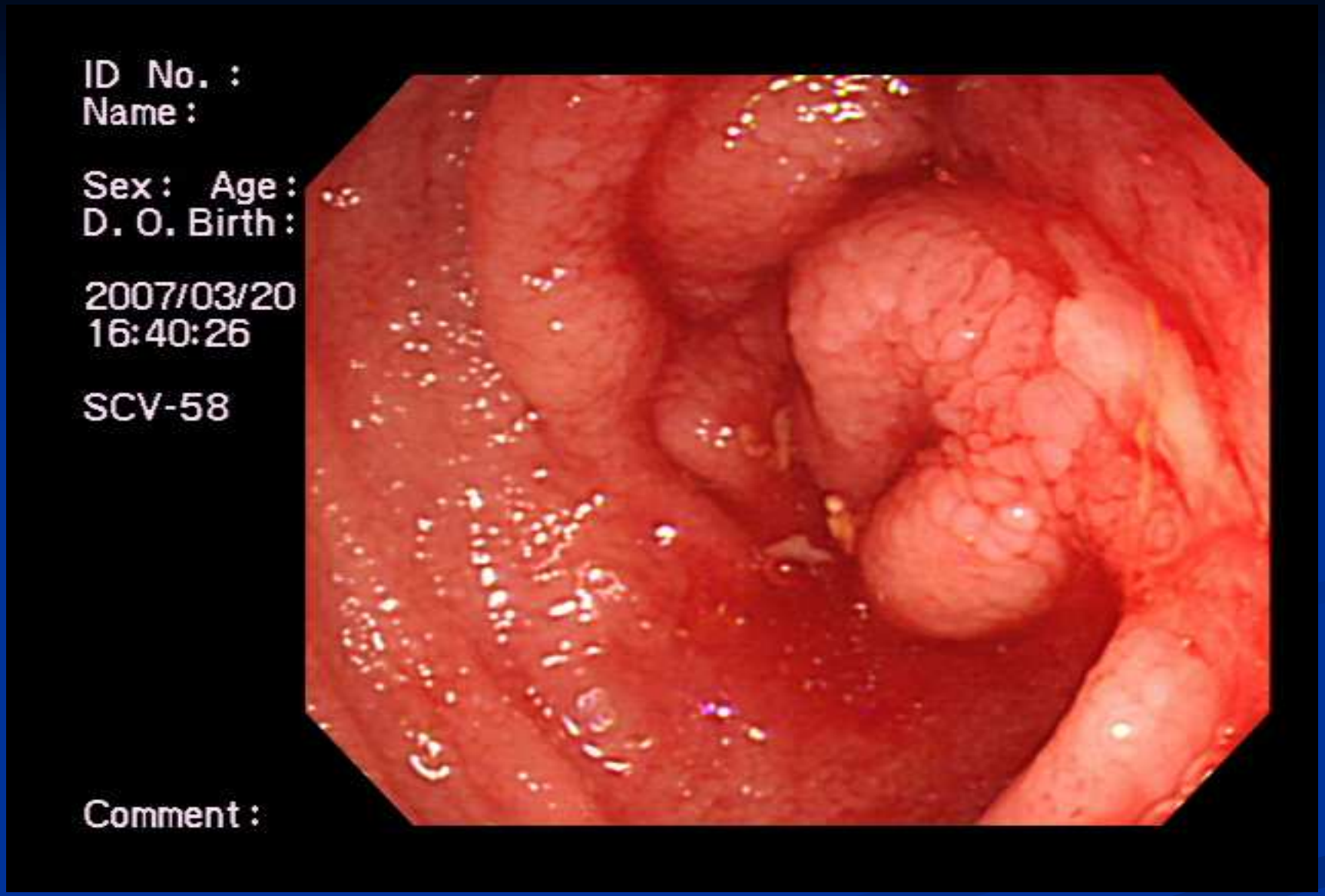
- Aphthous ulcer
- Longitudinal and transverse ulcers.
- Large, deep, penetrating ulcers can be surrounded by areas of normal-appearing mucosa
- “Skip lesions”
- Presence of fistula.
- Cobblestone appearance.
- Narrowing of the lumen.
- The rectum may or may not be involved.
- Hyperemia, edema, and loss of vascular pattern.



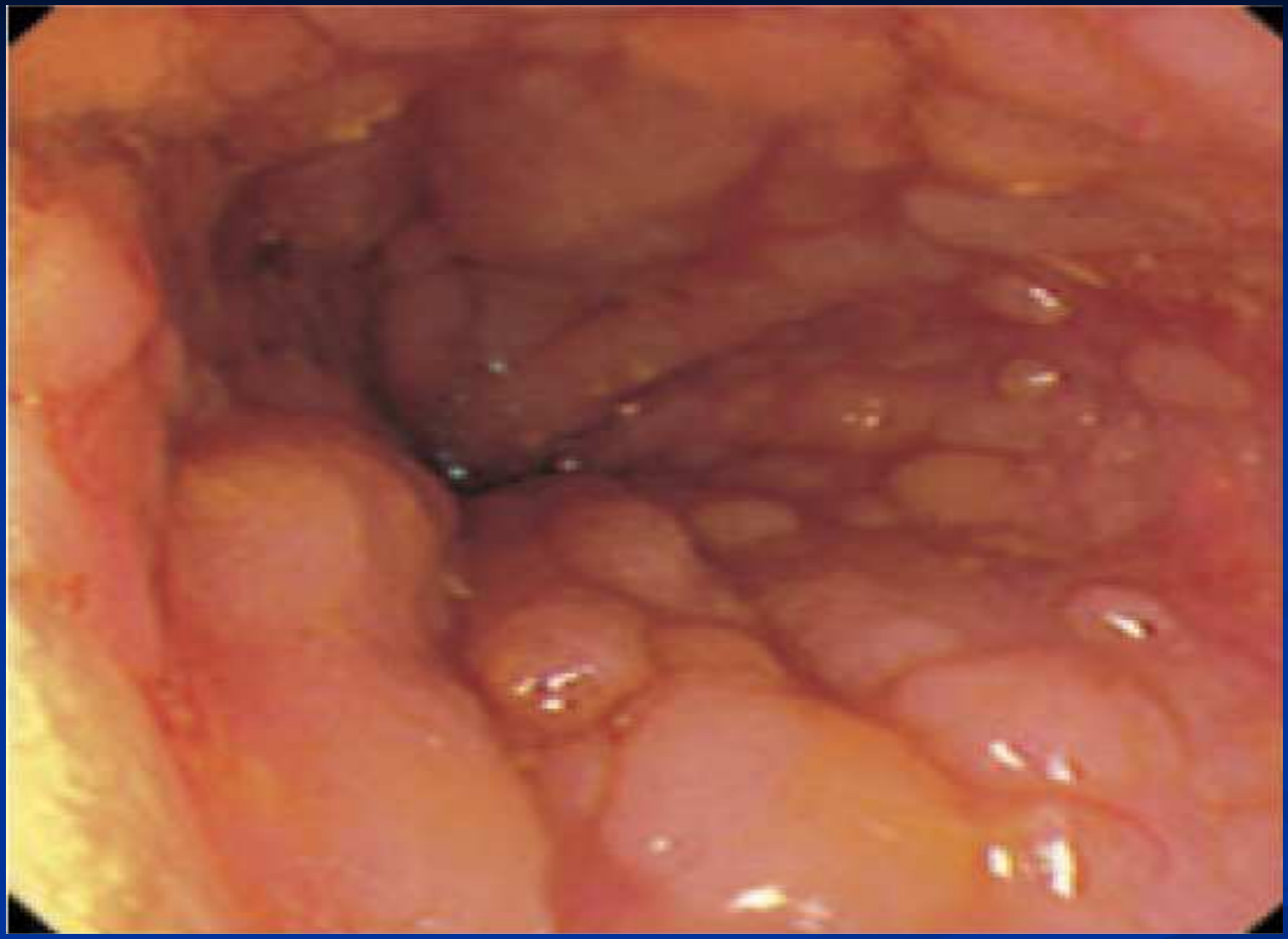
Female patient, 23 year with active Crohn's disease. Colonoscopic examination revealed colonic fistula



Colonoscopic examination revealed longitudinal ulcers



Crohn's disease.
Longitudinal ulcer in terminal ileum



Crohn's disease of the colon shows “cobblestone” appearance

Diagnosis

- **Differential diagnosis**
- Ulcerative colitis
- Infections
- Infections with Shigella, Amoeba, Giardia. Diarrhea has limited to a period of days to a few weeks. Stool cultures for pathogens and Serologic tests.
- Pseudomembranous colitis.
- Collagenous colitis.
- TB in terminal ileum.
- Diverticulitis.
- Intestinal lymphoma.

Medical Management

It is difficult to develop generally applicable guidelines for the management of Crohn's disease because of the great variety of anatomic locations, clinical manifestations, and gastrointestinal complications such as fistulas, abscesses, strictures, and perforations.

Medical Management

- **Active disease**
- For colonic Crohn's disease oral corticosteroids are first-line therapies.
- In patients with small bowel Crohn's disease, either prednisone or budesonide are appropriate.
- After the symptoms are controlled, prednisone can be gradually tapered until fully withdrawn from it
- 5-ASA preparation should be added to increase the likelihood of successful corticosteroid withdrawal.
- Before corticosteroids are given to a patient with abdominal pain, fever, and a high leukocyte count, an abdominal CT should be obtained to exclude an abscess.

Medical Management

- **Active disease-cont.**
- For corticosteroid-dependent patients, trial of an immunomodulator (6-MP or azathioprine) should be considered.
- Infliximab is typically given in combination with azathioprine or 6-MP to patients who have failed therapy with azathioprine or 6-MP.
- The approach to severe Crohn's disease is similar to the approach to severe ulcerative colitis.
- Patients with severe CD who do not respond to parenteral corticosteroids within a week should be considered for surgery

Medical Management

- **Active disease-cont.**
- **Anti–Tumor Necrosis Factor Antibody:**
- Infliximab, antibody against TNF-α, is effective in the management of active, moderate to severe CD and fistulas associated with CD, as well as in patients with refractory UC.
- Treatment is by intravenous infusion (5 mg/kg), which can be performed every 8 weeks or on an as-needed schedule.
- About 65% of patients with active CD improve, and about a third achieve remission.
- Long-term response rates, however, are considerably lower.
- Infliximab is associated with a substantial risk for infection (sepsis, pneumonia, and activation of tuberculosis) and a small but real risk for lymphoma, so it is generally reserved for patients who have failed to respond to azathioprine.

Medical Management

- **Maintenance Therapy**
- Maintenance therapy with aminosalicylates has been recommended for those brought into remission with corticosteroids or by surgery.
- The efficacy of aminosalicylates as maintenance therapy is much less well established in CD than in ulcerative colitis.
- Maintenance with 6-MP or azathioprine is recommended for
  - Patients brought into remission with these drugs or by surgery.
  - Corticosteroid dependent and then converted to these drugs.
- No role for corticosteroids as maintenance therapy.

Surgical Therapy

- Surgical resection is not curative of Crohn's disease and recurrences are likely.
- Therefore the approach is more conservative in terms of the amount of tissue removed
- Failure of medical management is a common cause for resection in patients with Crohn's disease.
- Complications (e.g., obstruction, fistula, abscess) are often indications for resection/ surgical therapy.

Treatment

- **Follow-Up**
- The risk for colon cancer in Crohn's colitis is less than in ulcerative colitis.
- The utility of surveillance in Crohn's colitis is unproven.

Thank you