

Inflammatory Bowel Disease

Calvary Public Hospital
GP Education Day
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Inflammatory Bowel Disease

- Ulcerative Colitis (UC)

- Recurring episodes of inflammation limited to the mucosal layer
- almost exclusively involves the rectum and may extend in a proximal and continuous fashion to involve other parts of the colon

- Crohn's Disease (CD)

- Transmural inflammation leading to fibrosis and strictures (→ obstructive symptoms); microperforations; fistulae.
- Skip lesions
- affects anywhere along the GI tract

Inflammatory Bowel Disease

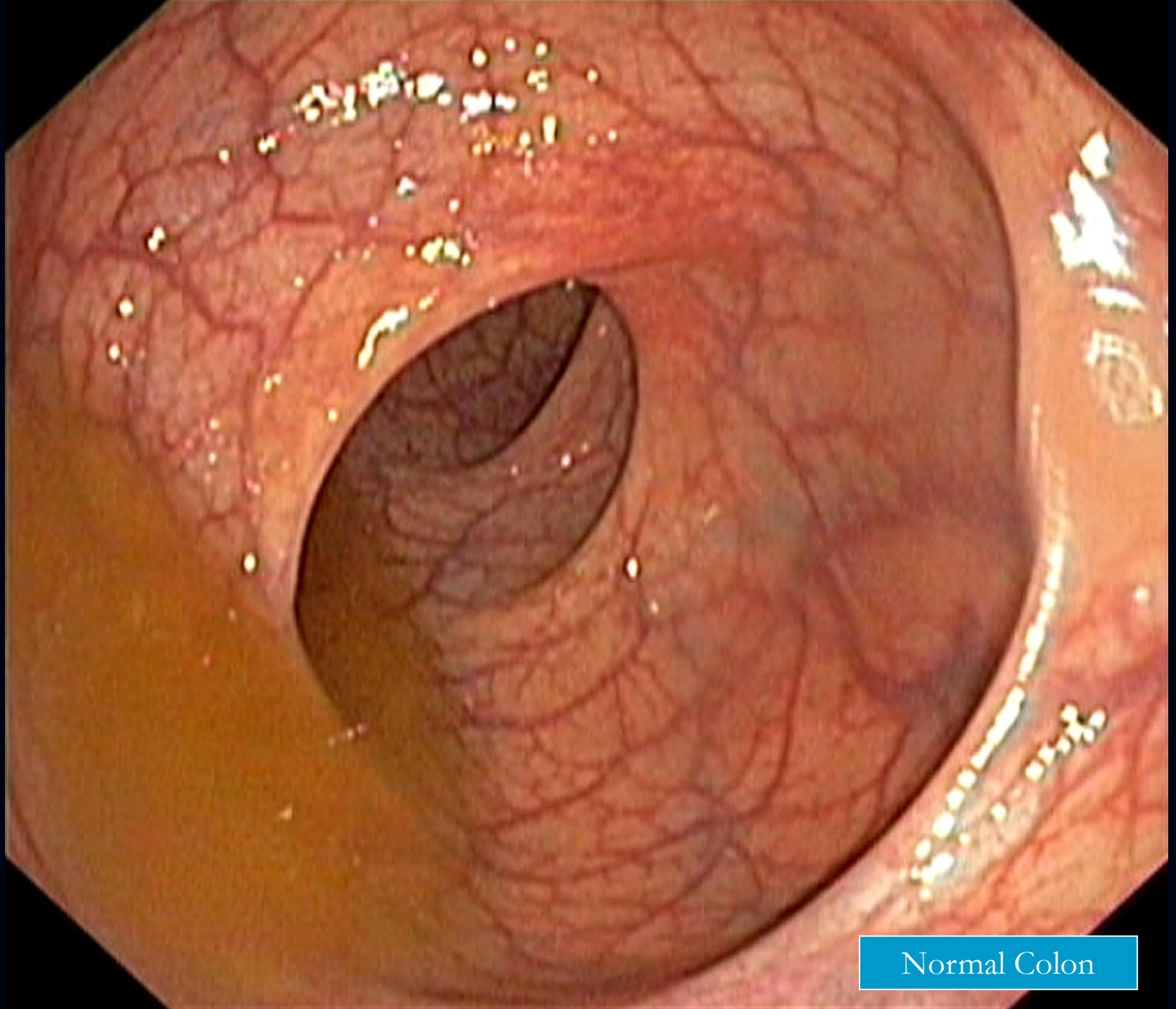
- Incidence of UC relatively constant over time
- Incidence of CD climbed between 1950's and 1980's, but is now relatively stable
- IBD prevalence varies racially and geographically
- Peak incidence 15-40yrs; possible second peak 50-80yrs
- Slight female predominance in CD
- Slight male predominance in UC
- 10-25% of patients have an affected 1° relative

Inflammatory Bowel Disease

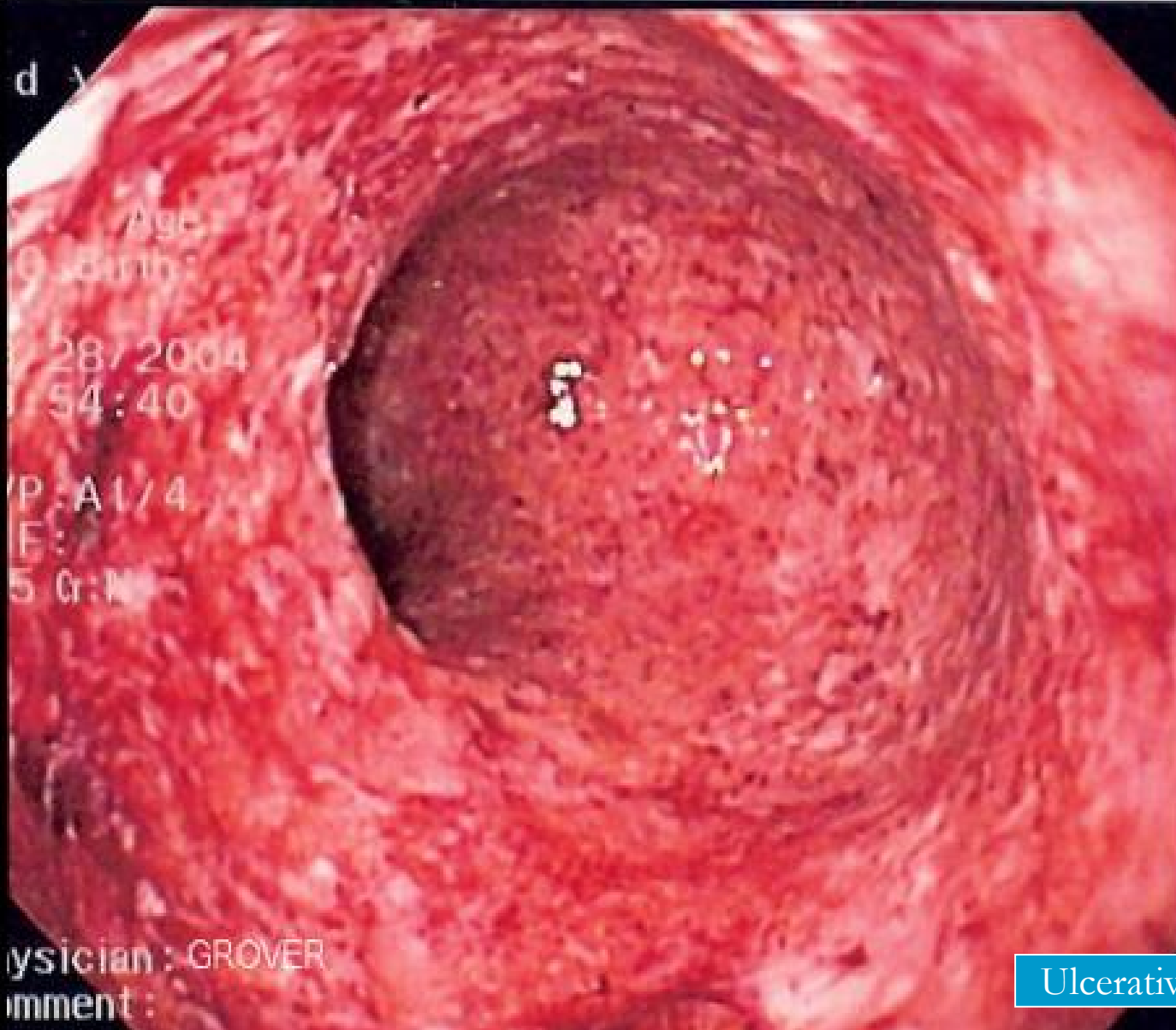
- Smoking increases the risk for CD but may be protective against UC
- Appendicectomy (<20yrs) may protect against UC
- Diet (processed, fried, sugary – ‘western’) are associated with an increased risk of CD and ?UC
- Obesity associates with increased disease activity and ano-perineal complications in CD
- Acute gastroenteritis, ‘health events’ in neo-natal period, use of antibiotics, NSAIDS, OCP, HRT possibly associate with IBD, but a causal connection unclear

Ulcerative Colitis

- Prevalence (USA) ~ 238/100,000
- Recurring episodes of inflammation limited to the mucosa
- Almost invariably involves rectum and may extend proximally in a continuous fashion
- May associate with peri-appendiceal inflammation and 'backwash ileitis'
- Usual symptoms – diarrhoea, blood, small volume and frequent stools, colicky pain, urgency, tenesmus, incontinence
- Occasionally patients may have constipation



Normal Colon



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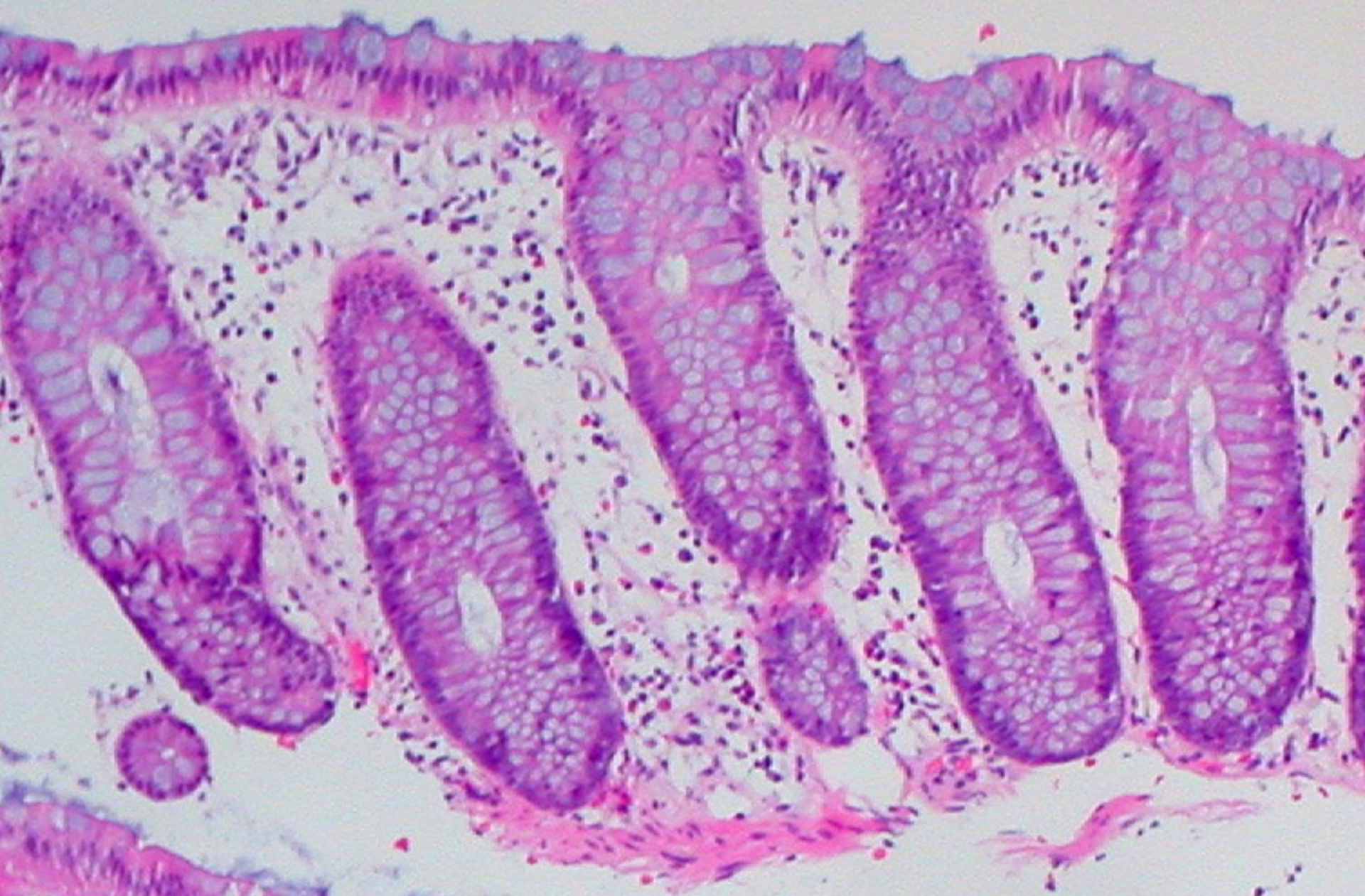
Age:
9.30m

28/2004
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P: A1/4
E:
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Physician: GROVER
Comment:

Ulcerative Colitis





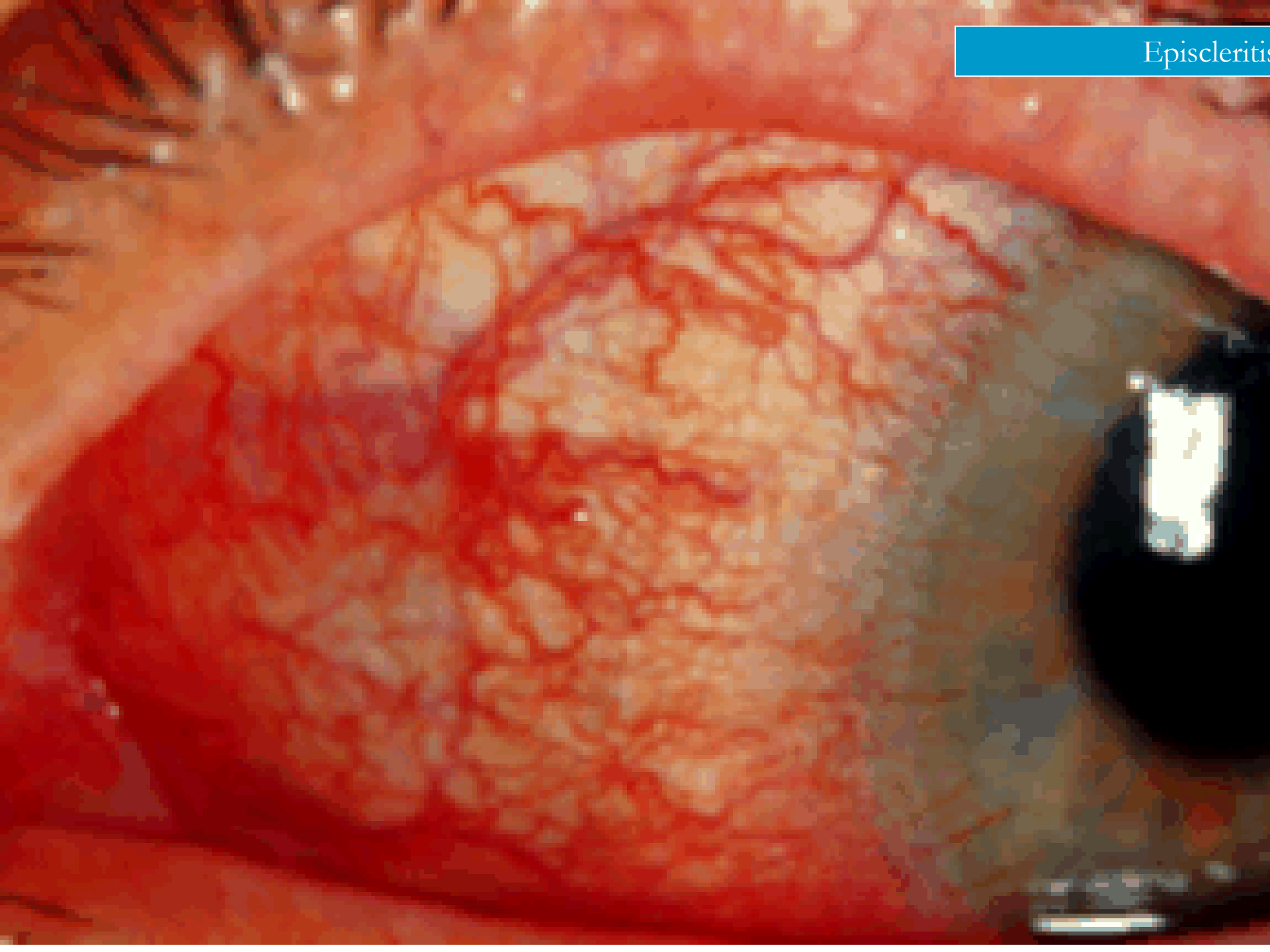
Inflamed Colon

Ulcerative Colitis

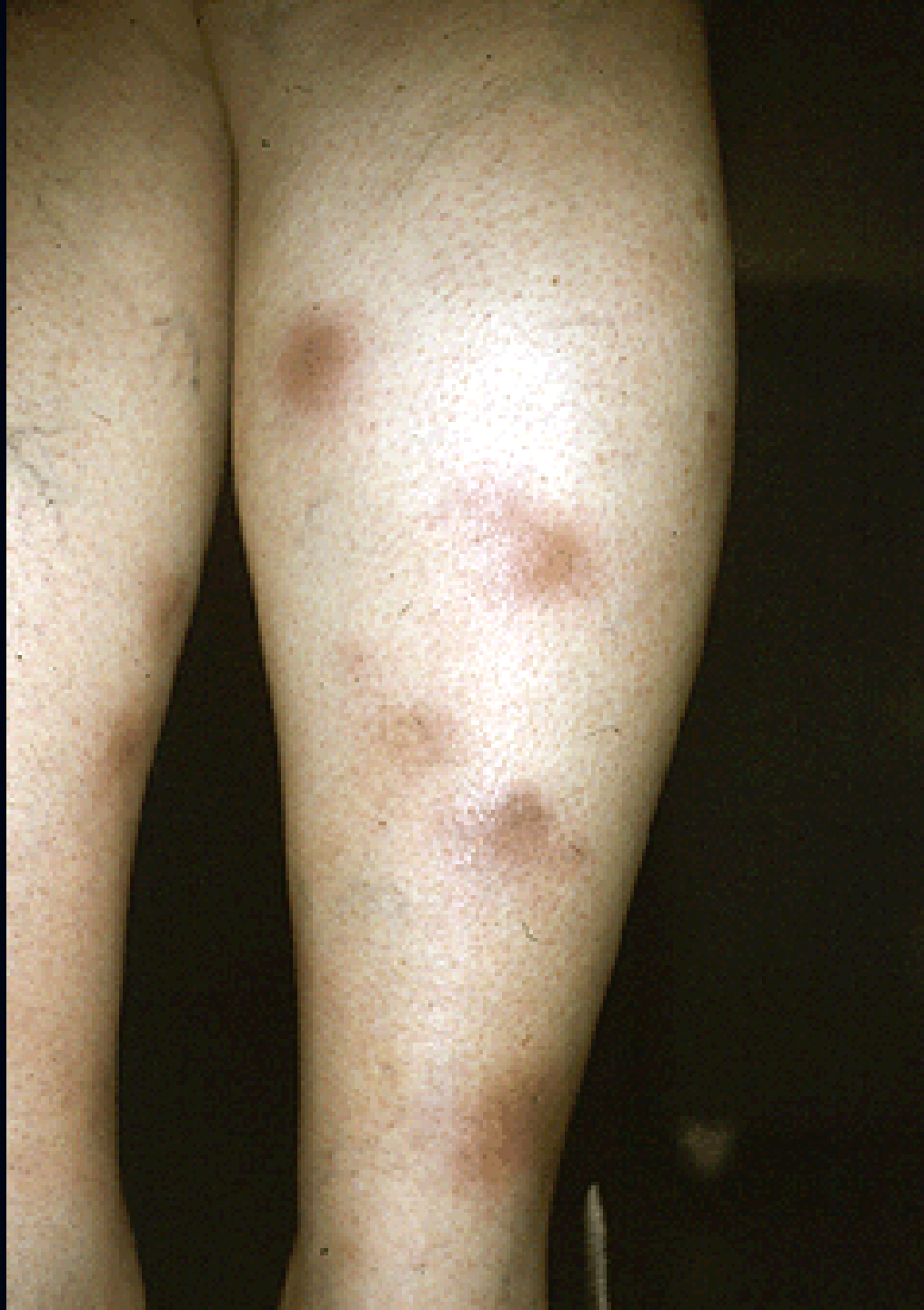
- Symptom onset usually gradual over weeks (vs acute and sudden)
- Ultimately ~ 20-30% of patients will require colectomy (is this reducing with modern treatment?)
- Up to 25% of UC patients will experience 'Extra-intestinal Manifestations (EIM)' in their lifetime
 - Musculoskeletal (peripheral arthritis; ank. spondylitis)
 - Eye (eg uveitis, episcleritis)
 - Skin (eg erythema nodosum, pyoderma gangrenosum)
 - Hepatobiliary (eg PSC, fatty liver, AIH)
 - Increased risk of venous and arterial thromboembolism

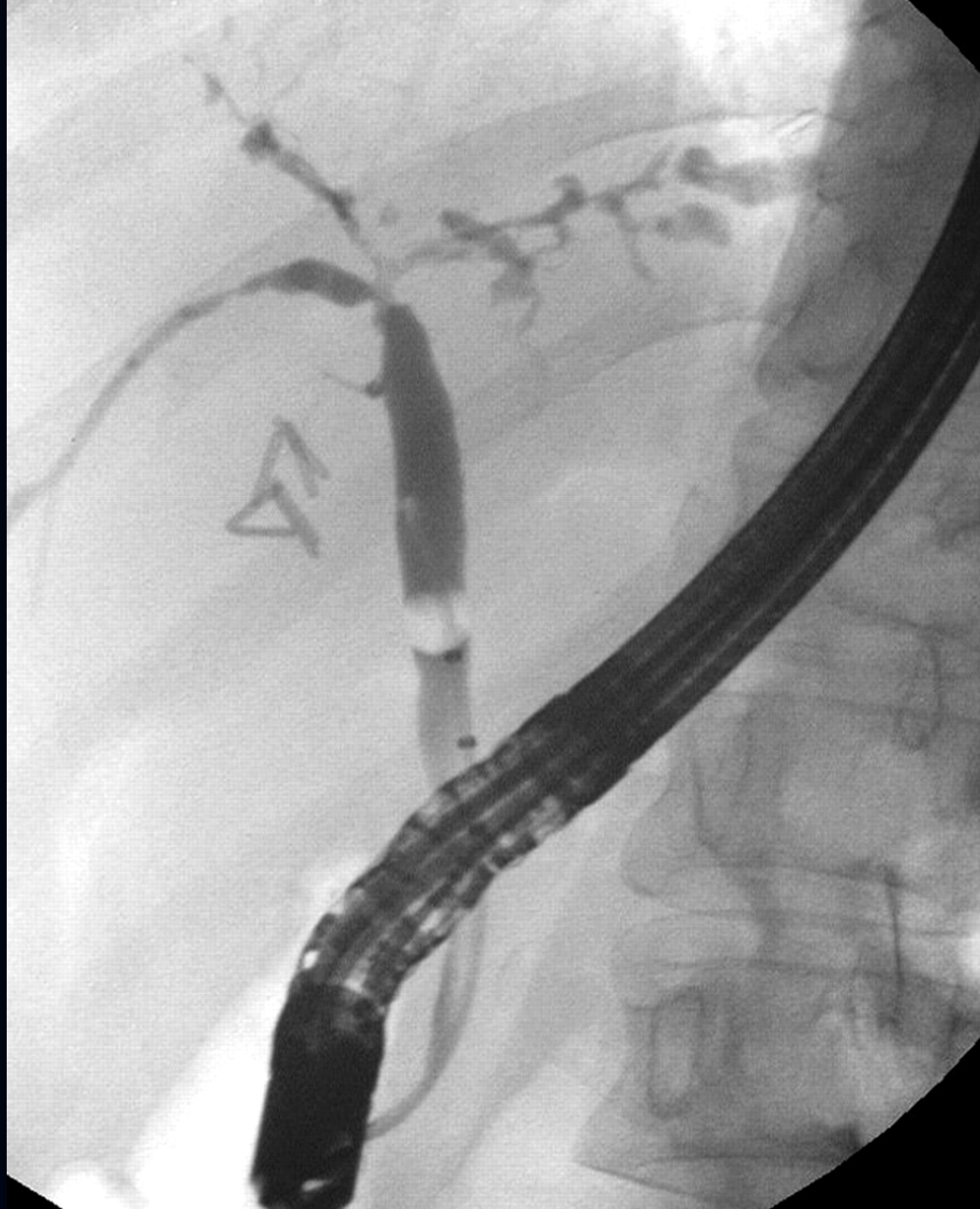
Uveitis













Ulcerative Colitis

- Complications
 - **Strictures**
 - **Dysplasia → Cancer**
 - Extensive disease ($> 1/3^{\text{rd}}$ colon affected)
 - Prolonged active disease
 - Disease duration $> 8-10$ yrs
 - concomitant FHx bowel cancer
 - Primary Sclerosing Cholangitis (PSC)*

Crohn(s) Disease

- Prevalence (USA) ~ 201/100,000
- Transmural inflammation (fibrosis, strictures, microperforations, fistulae)
- Skip lesions
- Can involve whole GI tract 'mouth to anus'
 - 80% have small bowel involvement (usually distal ileum)
 - 50% have ileocolonic involvement
 - 20% have disease limited to colon
 - 33% have perianal involvement

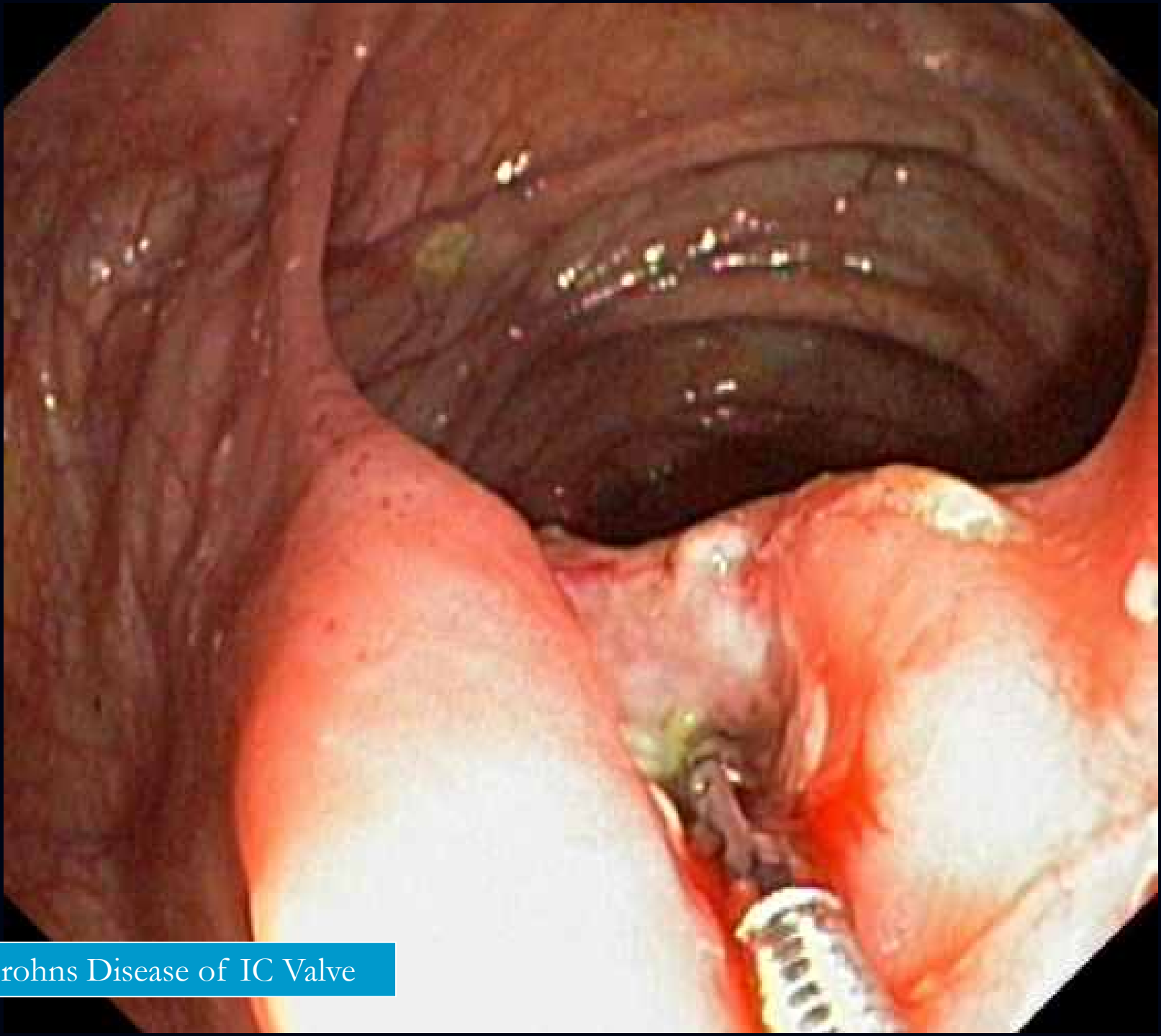
Crohn(s) Disease

- Symptoms include fatigue, weight loss, fever, abdominal pain, diarrhoea (but not necessarily overt bleeding)
- Symptoms generally more variable than with UC
- Extraintestinal manifestations (EIM) more common with colonic involvement and include those listed for UC and also:
 - Amyloidosis
 - Bone loss/osteoporosis
 - B12 deficiency
 - Gallstones

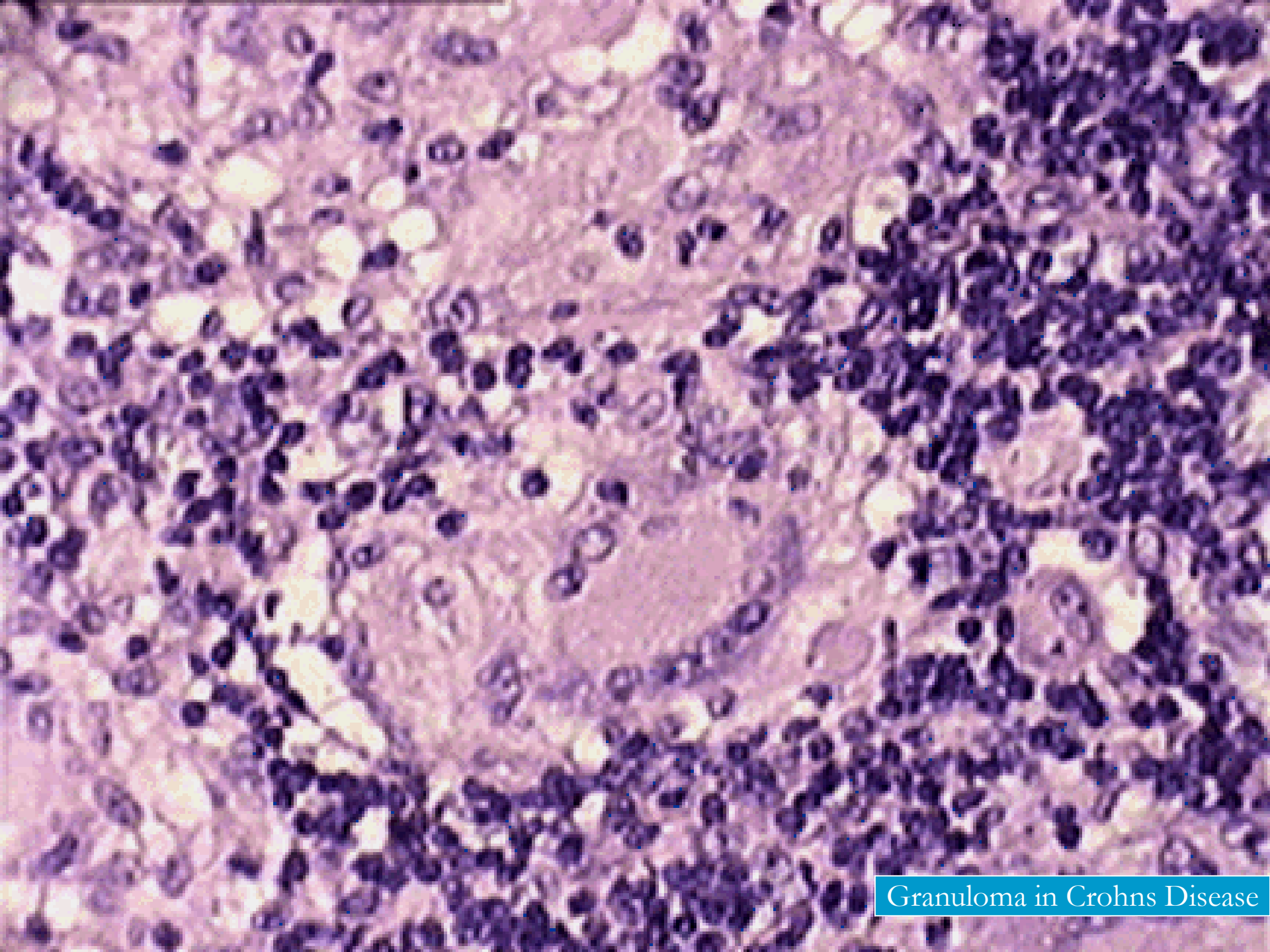
Crohn(s) Disease

- **Prognosis**
 - As with UC it is unclear if CD reduces life expectancy – if so, not by much
- **Risk factors**
 - Genetic susceptibility
 - Smoking
 - Diet
 - Sedentary lifestyle
 - ?Obesity
 - Dysbiosis



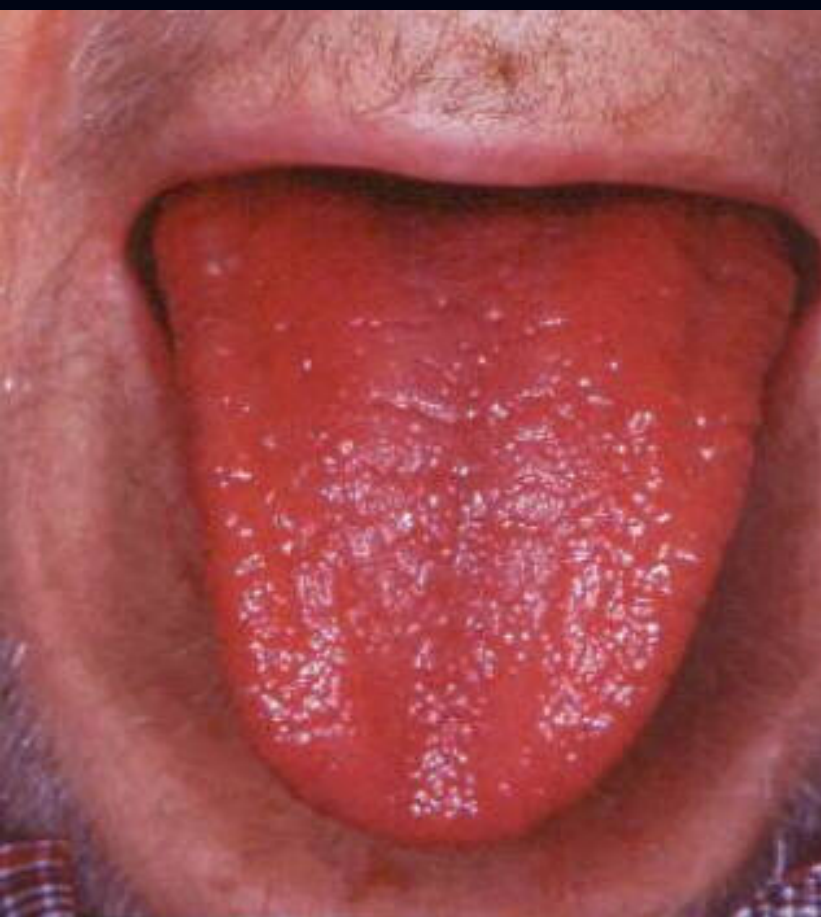


Crohn's Disease of IC Valve



Granuloma in Crohn's Disease





IBD - Management

- Lifestyle factors
- 5-ASA Medications
- Topical rectal treatments
- Oral Steroids
- Immunomodulators (Thiopurines/Methotrexate)
- Biologic Agents (Infliximab/Adalimumab/Vedolizumab)
- Microbiota manipulation (eg Faecal flora transplantation)
- Surgery

IBD - Management

- Lifestyle factors
 - Diet
 - Smoking
 - Exercise
 - ?Optimising weight
 - Sleep
 - ?Stress management
 - Avoid possible triggers (eg NSAIDS)

IBD - Management

- 5-ASA Medications

- **Sulphasalazine (SPZ)**

- ~10% do not tolerate
- 3 x 500mg tablets bd
- Very effective in mild to moderate UC; especially useful at maintaining remission and may reduce dysplasia risk
- Unclear if has much use in CD – although may help (+/- placebo response) in mild CD

- **Mesalazine/Olsalazine**

- Good alternative to SPZ
- Optimum dose 4-4.8g/ day; may use half that dose in stable patients in remission
- Can take as a single daily dose, irrespective of food

IBD - Management

- Topical rectal treatments
 - **5-ASA supps/foam enemas/liquid enemas**
 - Supps good for distal proctitis
 - Foam enemas good for recto-sigmoid disease
 - Liquid enemas good for left-sided disease, but may miss distal rectum (therefore, consider concomitant suppository)
 - Can use more than once per day, then wean as symptoms improve
 - **Steroid supps/foam enemas/liquid enemas**
 - Can be helpful; generally not as good as 5-ASA drugs (esp in UC)
 - Beware systemic absorption
 - **Others** (Arsenic, Tacrolimus etc)

IBD - Management

- Oral Steroids - the devil!
 - Work rapidly and well in UC/CD usually
 - Lots of short-term and long-term side-effects
 - Strong focus on keeping courses to a sensible length and using infrequently
 - If needing a lot – should consider alternative disease suppression treatment
 - Goal is a steroid-free remission



IBD - Management

- **Immunomodulators**

- Azathioprine (or 6-Mercaptopurine(6-MP))

- Consider checking TPMT enzyme activity before using
 - Usual maximum dose is ~ 2.5mg/Kg; 20% don't tolerate
 - Taken in one daily dose
 - Risks
 - Sepsis
 - Myelosuppression (\downarrow WCC; \uparrow MCV)
 - LFT disturbance
 - Pancreatitis
 - Non-melanoma skin cancer risk
 - Lymphoma risk
 - Can measure metabolites (6-TGN and 6-MMP)
(and manipulate metabolism with Allopurinol)

IBD - Management

- Immunomodulators
 - Methotrexate
 - Some value in CD
 - Lesser use in UC
 - Oral (up to 20mg/week) or IM/SC to 25mg PER WEEK
 - Folate supplementation required
 - Risks
 - Teratogenicity
 - Usual side-effects (sepsis, pulmonary injury etc)

IBD - Management

- Biologic Agents
 - Infliximab (Remicade or Inflectra)
 - Adalimumab (Humira)
 - Vedolizumab (Entyvio)
 - *Ustekinumab (Stelara)
- Government restrictions apply
- Most effective agents for IBD
- IV or SC delivery
- Generally reserved for most severe or intractable cases – but may be appropriate to use earlier
- Can measure trough levels / neutralising Ab levels and potentially dose adjust

IBD - Management

- Microbiota manipulation (eg Faecal flora transplantation)
 - Topical
 - Several trials in UC (including one from Australia)
 - Mixed results
 - ?identifiable 'super donors' who give the best results
- Comes on a background of growing interest in the role of the microbiome in disease causation (IBD/IBS and others)
 - Our understanding is poor but it seems that good diet/exercise influence the microbiome for the better
 - a mixed and varied microbial flora (vs a restricted flora) connotes less disease

IBD - Management

- Surgery

- Still has an important role in both UC and CD
- Moderate to severe or fulminant UC unresponsive to medical therapy may still require colectomy
 - Thereafter issues with stoma or pouch have to be considered
- Ileocaecal stricturing from localised CD may be best treated by surgery (perhaps without any medical therapy)
- Strictures/perforations/abcesses/fistulae
- Colectomy may be necessary with extensive colonic dysplasia or cancer in both UC and colonic CD.

Other Issues to consider

- **Vaccination**

- VZV (live attenuated – beware)
- Hep A & B
- Pneumococcus
- HPV
- Annual 'flu/H1N1 'flu
- (beware live attenuated organisms in newborns of mothers receiving biological drugs)

- **PAP Smears**

- Cervical dysplasia increased in patients on Immunosuppression
- ?age at which to vaccinate against HPV

Other Issues to consider

- Conception/Pregnancy

- IBD should be no barrier
- Best if conception/pregnancy occurs when disease well controlled and in remission
- Avoid Methotrexate
- Usual other IBD drugs can generally be used with relative safety
- Give last dose of Biologic drug such that maternal serum levels are at their lowest ebb just before expected delivery date – so newborn has lowest blood levels
- Caesarean section preferable in women with significant crohns-related peri-anal disease

Other Issues to consider

- Management of Osteoporosis
- Maintenance of nutrition
- Management of depression
- Fertility/Pregnancy/Lactation
- Management of co-existent IBS

Summary

- Increasingly complex treatment options for IBD Patients
- Use 5-ASA drugs to optimal effect in UC
- Limit Steroid exposure
- Optimise thiopurine dosage, manipulate drug metabolism (Allopurinol) and be mindful of short and longterm side-effects
- Know about the growing array of Biological drugs
- Vaccinate early



Toying with Human
Motions