

A clinic for challenging Candida infections

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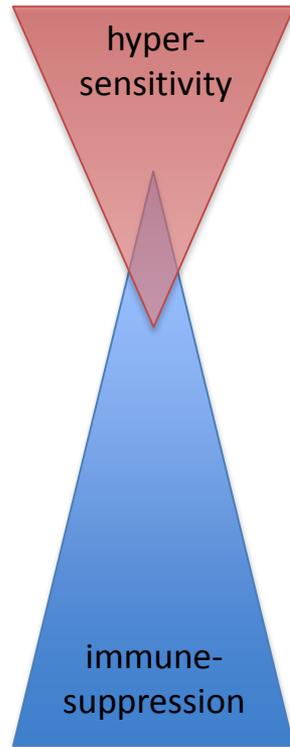


Illustration: Dan Smith

***Candida* is part of normal flora**

- oral cavity
- gut
- vagina
- moist areas of the skin
- airways

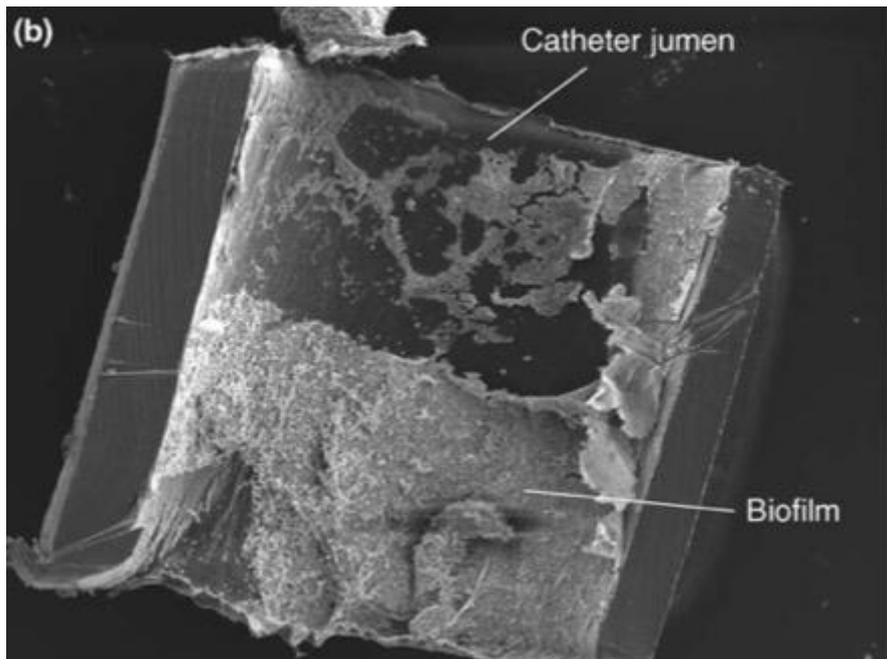
Candida may cause



- *Candida* vulvo-vaginitis
- *Candida* balanitis
- Oral candidosis
- Skin and nail infections
- Sepsis and disseminated disease

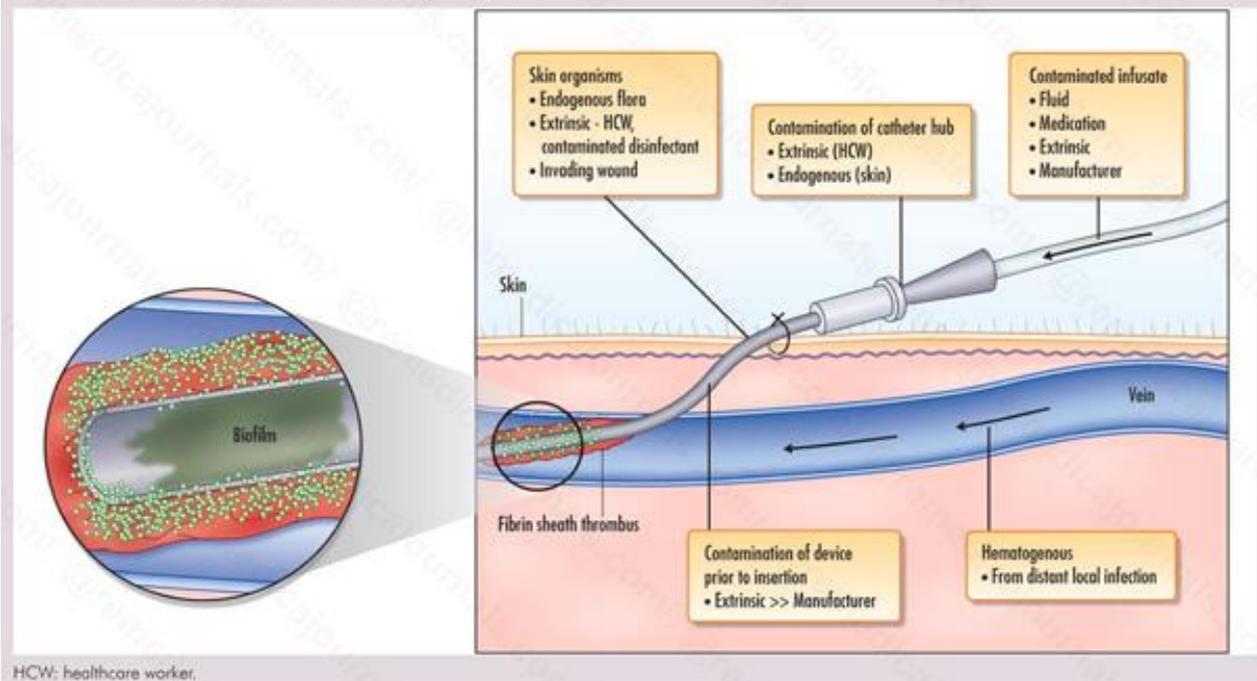
Candida prefers to grow as a biofilm

- *Candida* can rapidly form biofilms in the human body: non-renewing surfaces, cavities.
- Biofilms are organised microbial communities that are innately resistant to antimicrobials and host immune mechanisms and cannot be treated with antimicrobials alone.
- They are a major source of recurrent, chronic and disseminated infections.



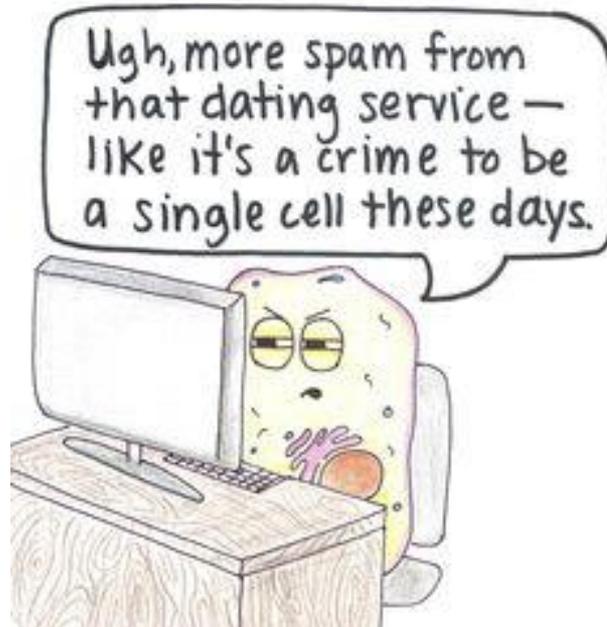
Intermediate life form between unicellular and multicellular organisms.

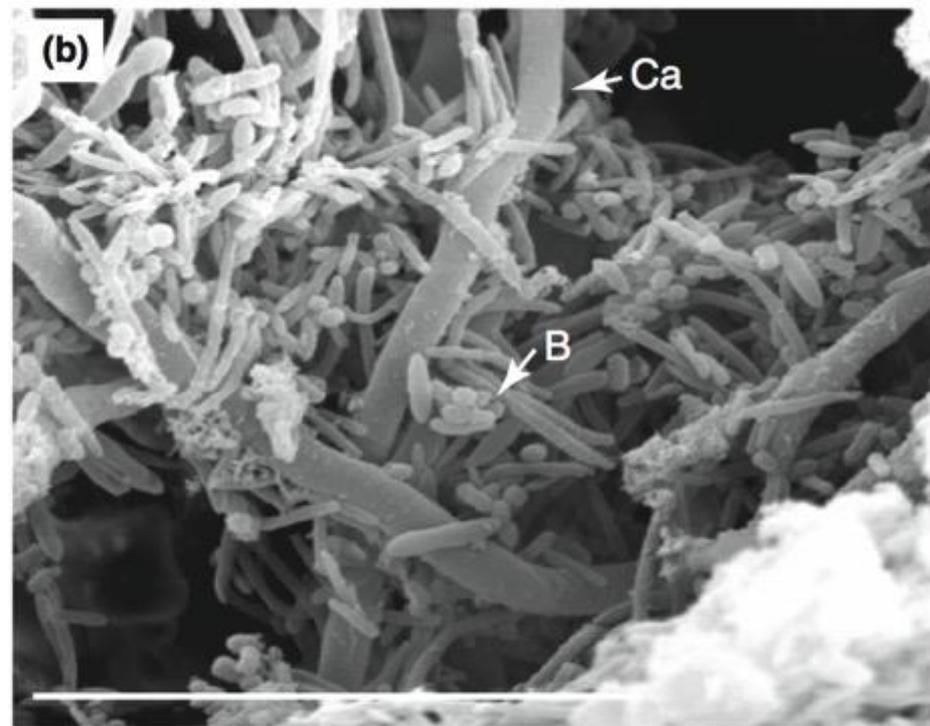
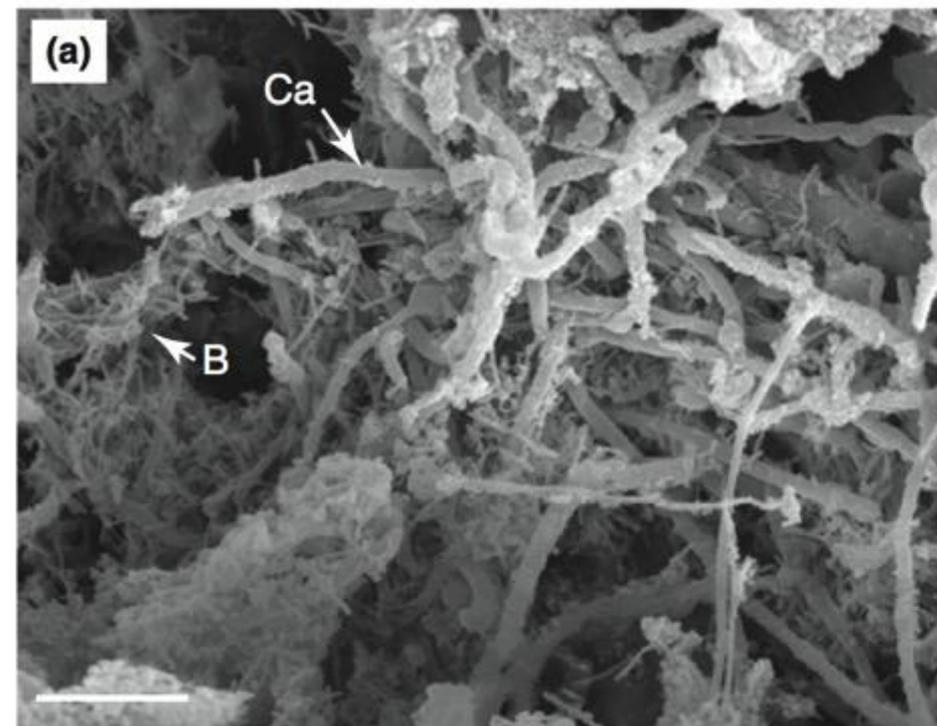
Figure 2. Diagram of an intravenous catheter with biofilm growth.



What is a biofilm?

- The gene expression of microbes change significantly when they adopt a biofilm life style
- The regulation of the expression of virulence genes is a crucial step in pathogenesis (quorum sensing).





TRENDS in Microbiology



Antibiotic



Antibody



Planktonic cells



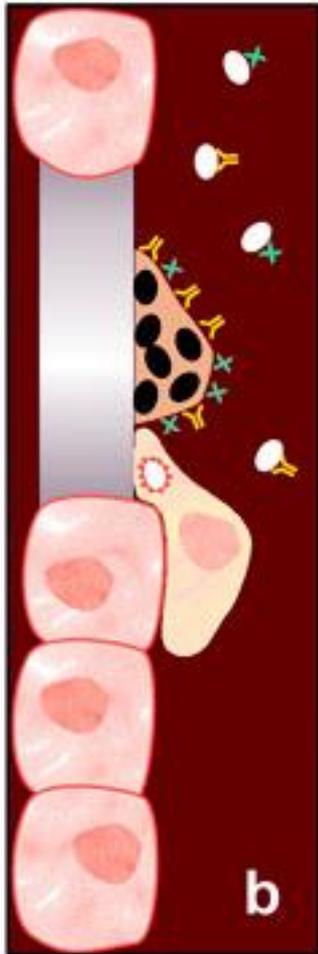
Biofilm cells



Phagocyte enzymes



a



b



c



d

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2603-99cs P. DIRCKX

A clinic for challenging *Candida* infections

- Recurrent vulvovaginal candidosis
- Recurrent oral/oesophageal candidosis
- *Candida* skin infections (CMC, CF)
- Recurrent *Candida* UTIs
- Candidosis as a secondary diagnoses (chronic underlying conditions: immunosuppression, DM, dermatological, chronic pain)
- Treatment resistant candidosis

Vulvo-vaginal candidosis (VVC)

- The clinical features of acute VVC including vulval itching, soreness, vaginal discharge, erythema, fissuring and oedema are **non-specific**; a number of other **infectious or non-infectious** conditions can present similarly.
- In the absence of clinical response to appropriate treatment it is important to consider revision of the diagnosis as **asymptomatic carriage is common** (up to 20% of women in childbearing age and up to 40% in pregnancy).
- *C. albicans*, rarely *C. glabrata*

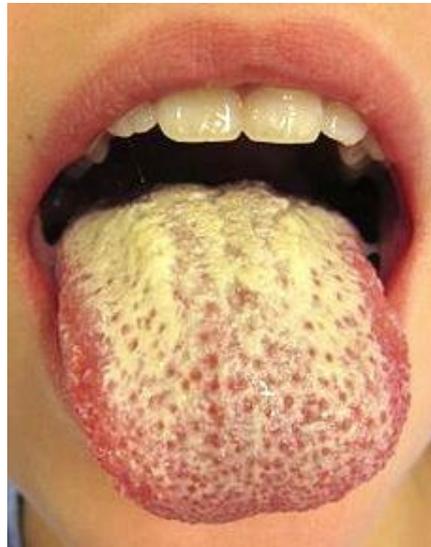
Vulvo-vaginal candidosis (VVC)

Even a **single attack** requires:

- Oestrogen > lactobacilli > pH
- Adherence, growth, ?invasion
- Host response:
 - allergic processes may be involved
 - complex immune interactions locally
 - neutrophils: proteolytic enzymes
- Sometimes complicated with recurrent BV

Single attack does not require predisposing factors but **recurrent disease is associated** with diabetes, MBL and other **immunological deficiencies and dysregulation.**

Acute oral candidosis



Chronic oral candidosis





Predisposing factors

1. Altered oral flora (Yeast favouring: antibiotic treatment, narrow spectrum mouthwashes, high alcohol consumption, reflux, low pH diet, artificial materials (dentures), diabetes)
2. Poor oral hygiene (biofilms)
3. Impaired local defence mechanisms (lack of saliva, inhaled steroids, smoking, radiotherapy)
4. impaired systemic defence mechanisms (Immunosuppressive medication, DM, malnutrition, primary or secondary immunodeficiency, HIV, genetic: AIRE / STAT1 mutations)

There must be a reason!

Oral Leukoplakia



Oral Lichen Planus



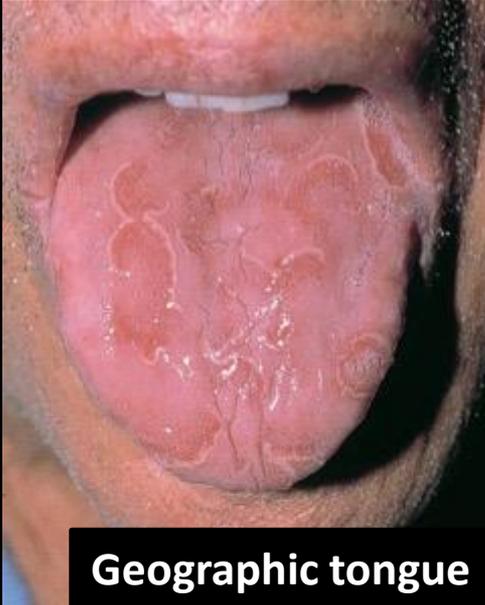
Oral Lichen Planus



Oral Leukoplakia



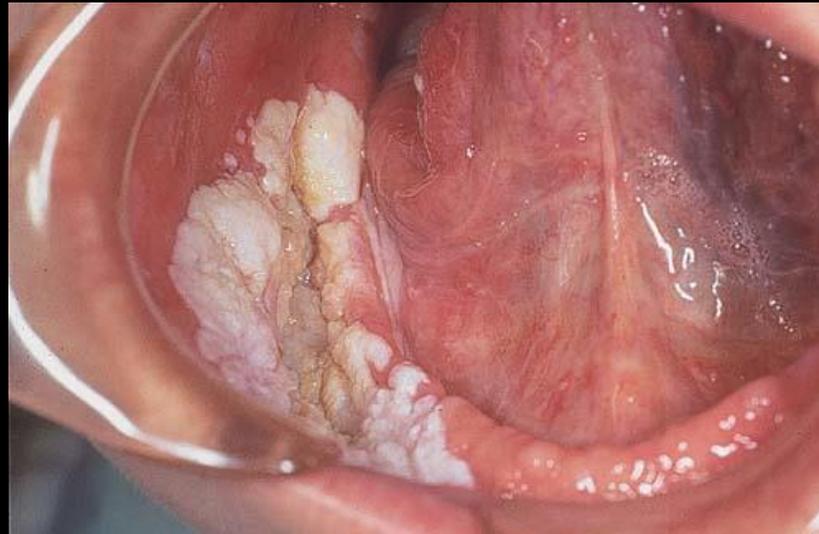
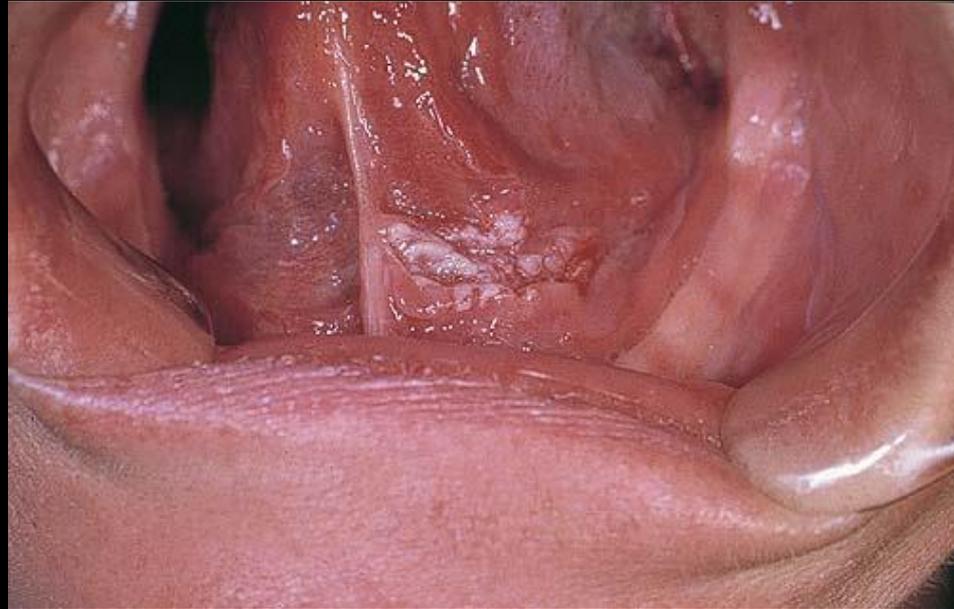
Geographic tongue



Chewing marks



Squamous Cell Carcinoma



APECED

- **Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED)** an autosomal recessive autoimmune disease due to a mutation in the AIRE gene and affects various endocrine glands.
- Most patients have chronic or recurrent oral candidosis since early childhood.
- Patients receive repeated treatment and prophylactic courses of antifungals throughout life and azole resistance is common.
- The chronic candidosis presents with leukoplacic and hyperplastic lesions as well as with atrophy.
- The chronic candidosis is potentially carcinogenic: 10% of the patients above the age of 25 have developed oral cancer at the site of chronic mucositis lesions and it is the only malignancy reported in these patients.

APECED (APS1; AIRE mutation)





Oral and oesophageal squamous cell carcinoma – A complication or component of autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED, APS-I)

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CMC (STAT1 mutation)



If thrush does not respond to treatment...

.... the diagnosis is probably wrong.

Cutaneous candidosis



CMC (STAT1 mutation)



Candida Urinary Tract Infections—Treatment

CID 2011:52 (Suppl 6) S457-466

John F. Fisher,¹ Jack D. Sobel,² Carol A. Kauffman,³ and Cheryl A. Newman¹

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Table 1. Predisposing Factors for Candiduria and *Candida* Urinary Tract Infections

Predisposing Factors
Diabetes mellitus
Renal transplantation
Extremes of age
Instrumentation of the urinary tract
Female sex
Concomitant bacteriuria
Prolonged hospitalization
Congenital abnormalities of the urinary tract
Intensive care unit admission
Structural abnormalities of the urinary tract
Broad-spectrum antibiotics
Indwelling urinary tract devices
Bladder dysfunction
Urinary stasis
Nephrolithiasis

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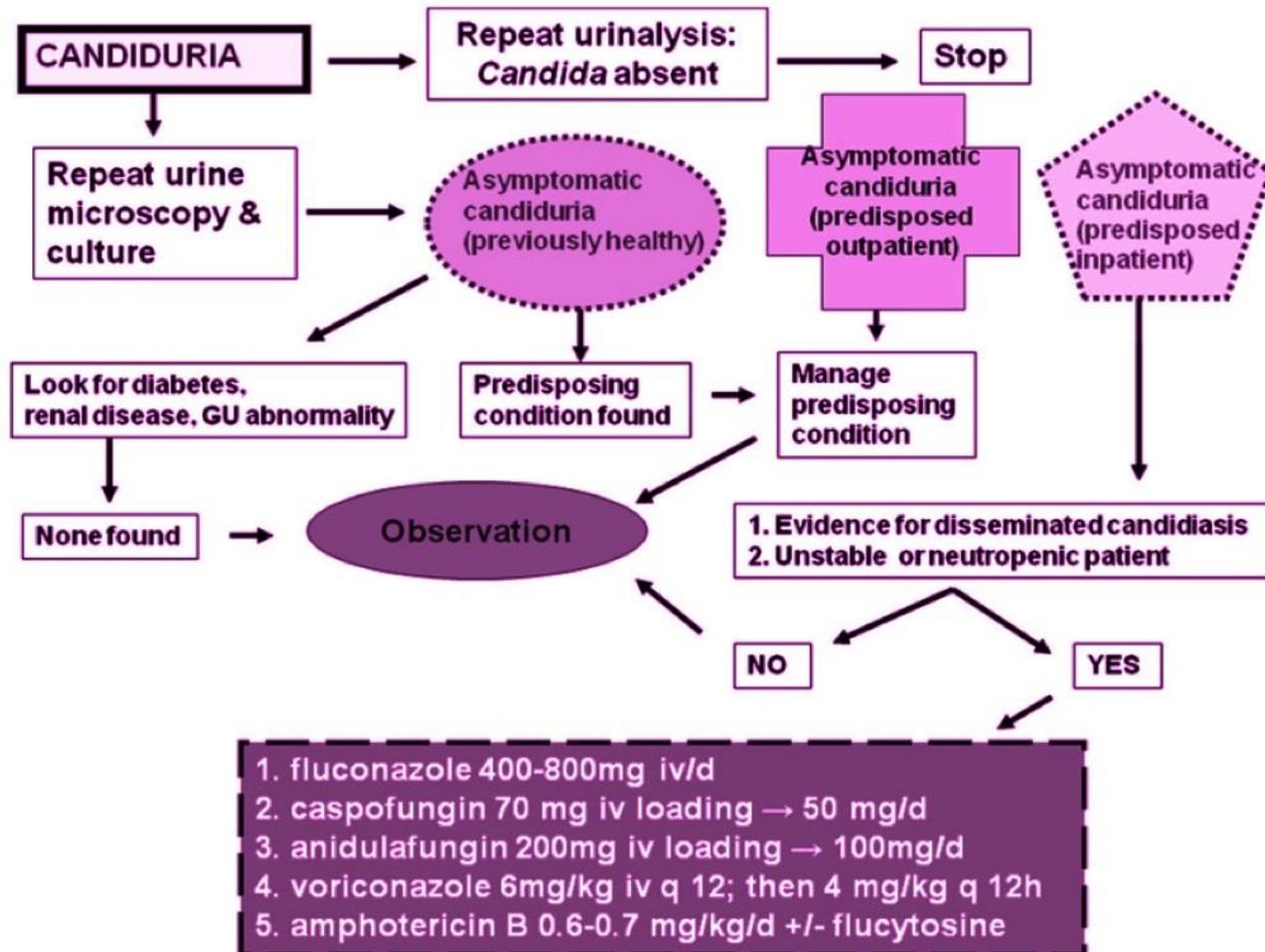


Figure 1. Algorithm for the management of asymptomatic candiduria.

What options do we have?

- **Fluconazole** is the first line treatment.
- **Flucytocine**: favorable pharmacokinetics in the urinary tract and proven efficacy in a variety of forms of urinary tract candidiasis. In long term therapy, needs combination with another antifungal to prevent resistance.
- **Conventional Amphotericin B**: effective but associated with significant kidney toxicity.
- **Lipid formulations of Amphotericin B**: should not be used for treating renal candidiasis due to reduced penetration into the renal parenchyma and failure to clear the urinary tract in reported cases.
- **Echinocandins**: efficient in the treatment of parenchymal infections but extensively metabolised and very little active drug can be detected in urine. A few case reports on successful use in patients with ascending *Candida* pyelonephritis.

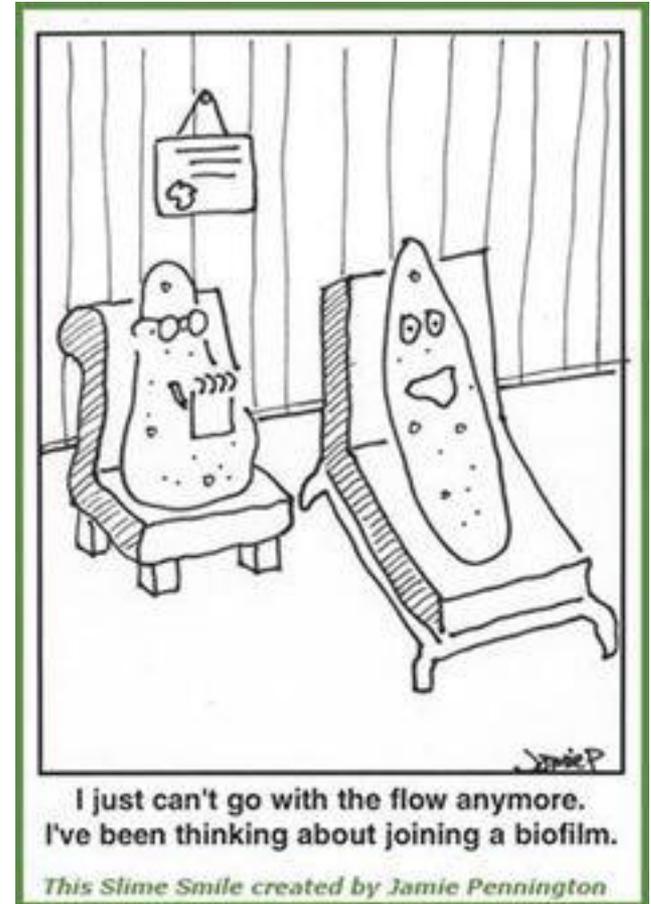
What options do we have?

- Fungal ball: most patients have been managed with surgical removal + systemic treatment with cAmB, with or without flucytosine, or fluconazole
- If urological procedure required (eg percutaneous nephrostomy providing an access to the renal pelvis, ureters, or bladder) local irrigation with intermittent or continuous cAmB or fluconazole can be considered, but studies to determine optimal dosage and duration have not been done.
- Bladder irrigations with cAmB are sometimes used in combination with surgical interventions

A clinic for challenging Candida infections



Illustration: Dan Smith



I just can't go with the flow anymore.
I've been thinking about joining a biofilm.

This Slime Smile created by Jamie Pennington