

Prevention of opportunistic infections in patients with inflammatory bowel disease

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OI: definition

An opportunistic infection may be defined as a serious and usually progressive infection by a micro-organism that has limited (or no) pathogenic capacity under ordinary circumstances, and that has been able to cause serious disease as a result of the predisposing effect of another disease or of its treatment

Infections are a cause of death in IBD

- Population-based study of mortality and cause of death in CD :

Standardized mortality ratio for infections :

8.3 (1.0-30.9) in women

2.1 (0.0-11.8) in men

- Population-based study of mortality and cause of death in UC :

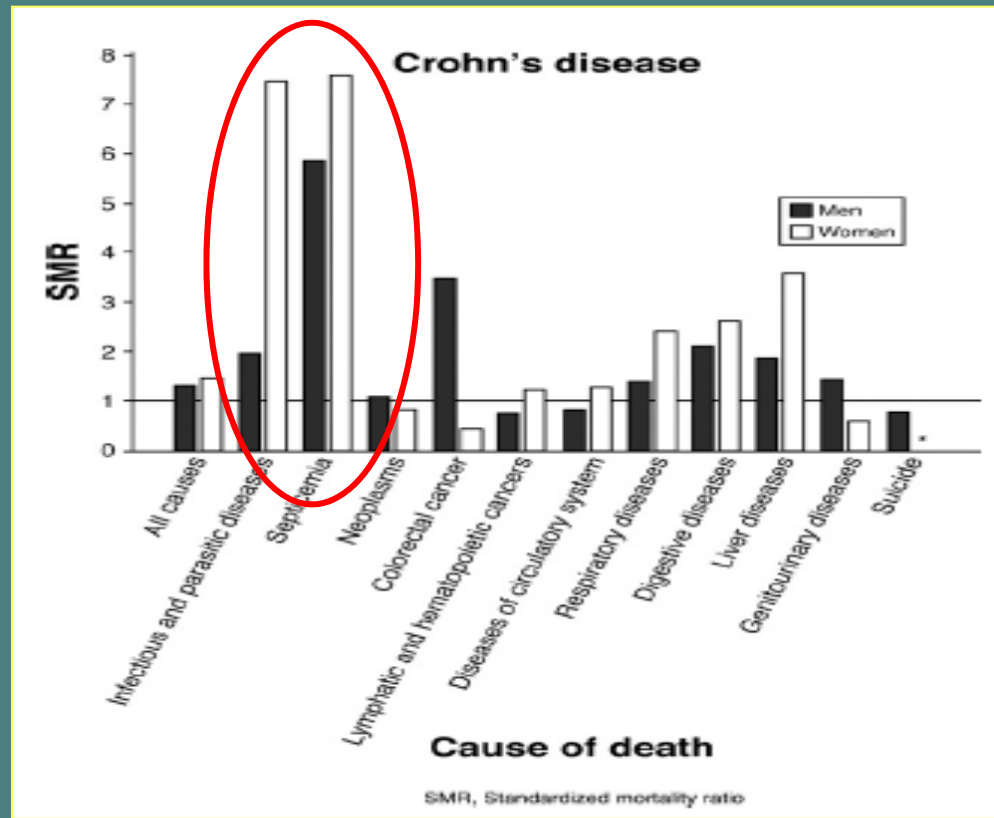
Standardized mortality ratio for infections :

3.3 (0.6-9.5) in women

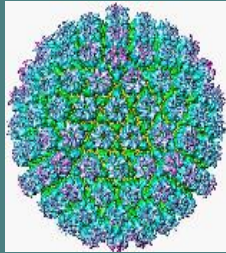
1.6 (0.33-4.7) in men

Infections are a cause of death in IBD

Mortality data from Kaiser Permanente N. California IBD Registry



After 2001 : case reports

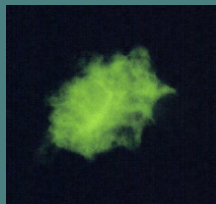


Herpes simplex
CMV
Varicella zoster
EBV
HPV

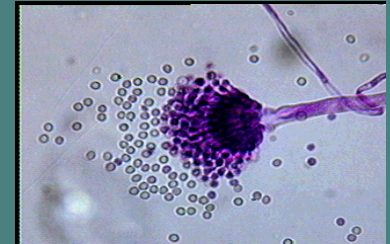
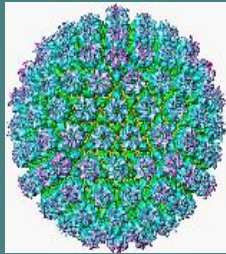
M. Tuberculosis
M. Avium sp.
M. Xenopi
Listeria monocytogenes
Staphylococcus sp.
Nocardia
E. Coli
Salmonella sp.

Histoplasmosis
Aspergillus spp.
Cryptococcus spp.
Candida spp.
Coccidioides immitis
Pneumocystis jiroveci

Strongyloides stercoralis
Toxoplasma gondii



Pathogens that cause death



~~Herpes simplex~~

CMV

Varicella zoster

EBV

~~HPV~~

M. Tuberculosis

~~*M. Avium sp.*~~

~~*M. Xenopi*~~

Listeria monocytogenes

Staphylococcus sp.

Nocardia

E. Coli

Salmonella sp.

Histoplasmosis

Aspergillus spp.

Cryptococcus spp.

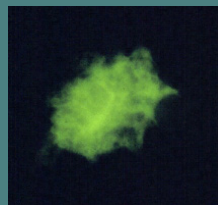
Candida spp.

~~*Coccidioides immitis*~~

Pneumocystis jiroveci

Strongyloides stercoralis

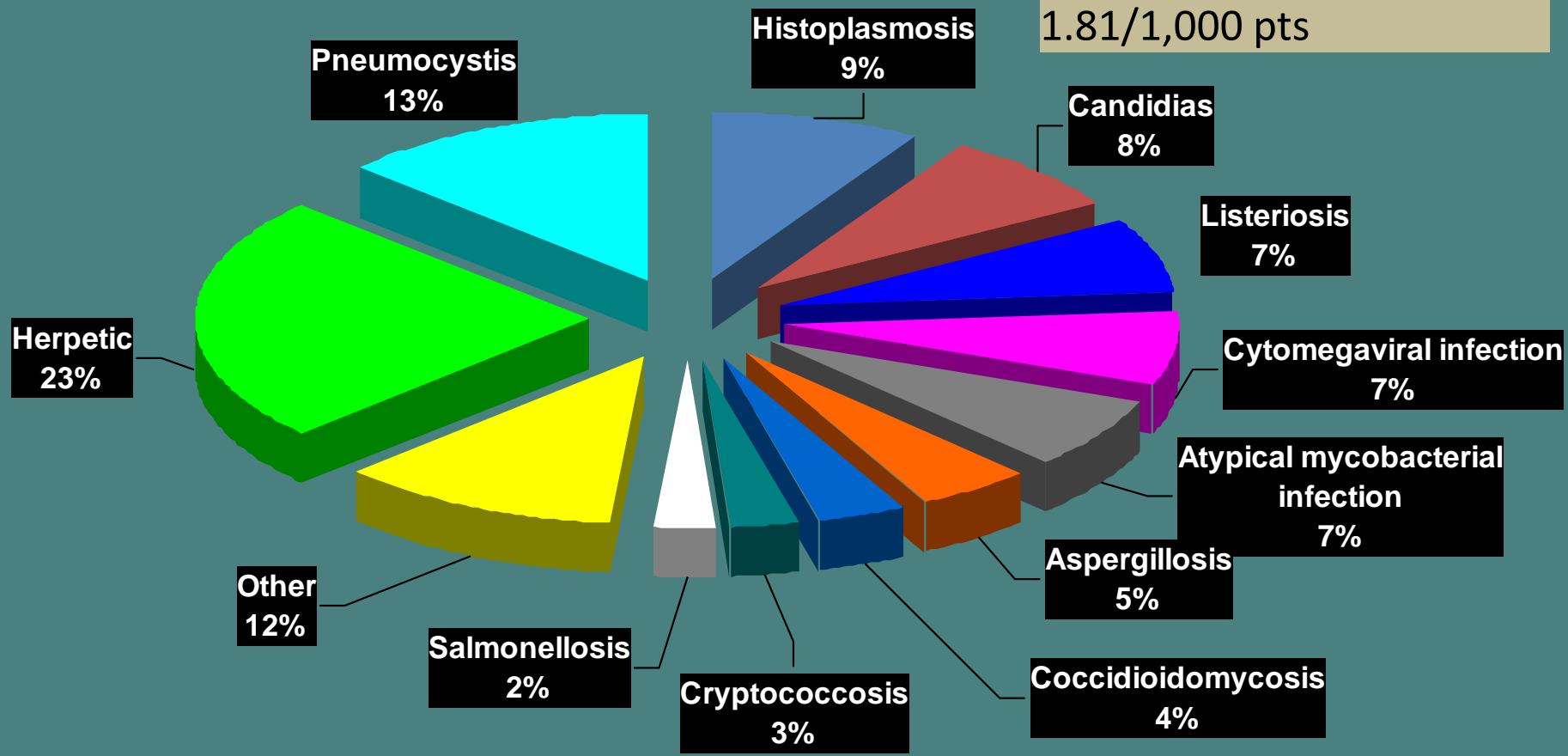
Toxoplasma gondii



Serious Opportunistic Infections: Cumulative Worldwide

Cumulative Since Launch: 24 Aug 1998-23 Aug 2008

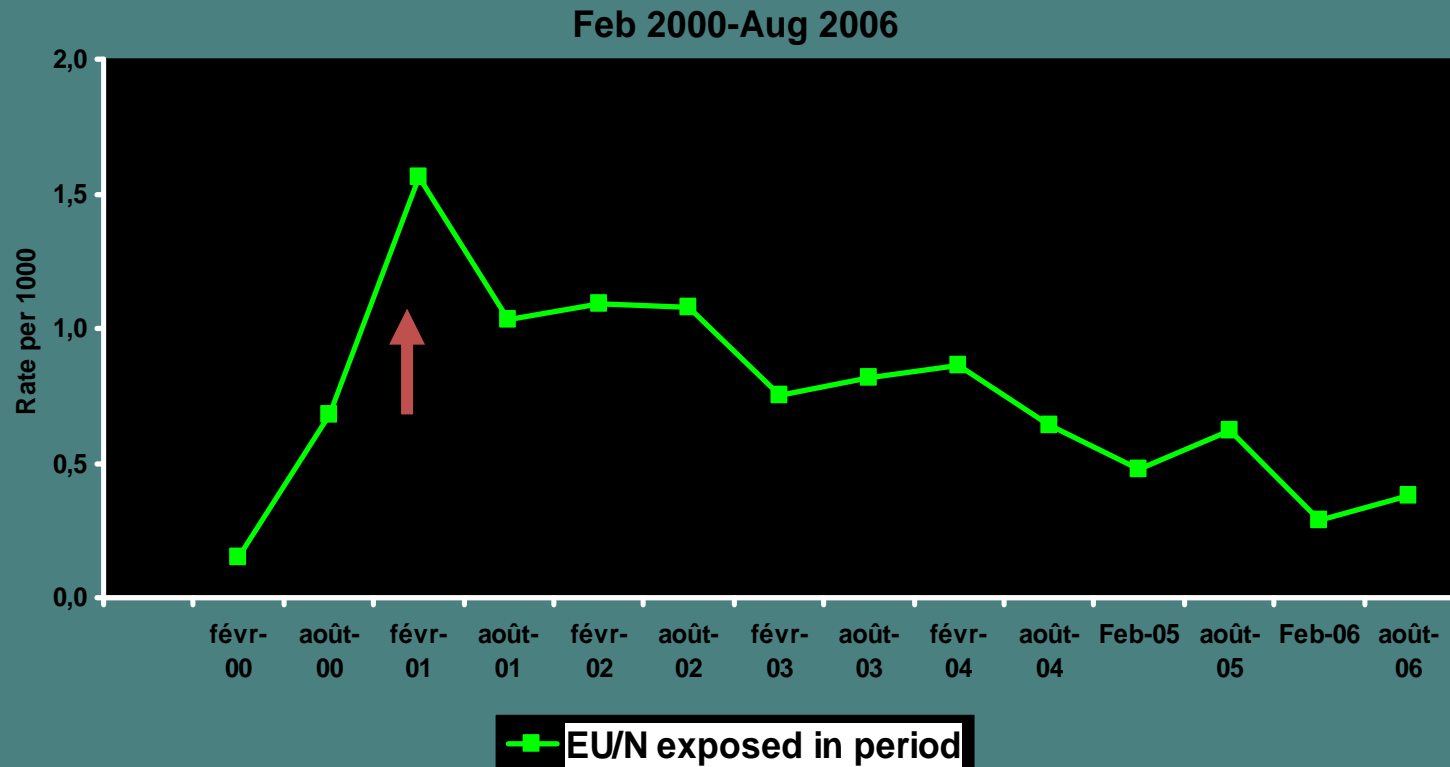
Overall Reporting Rate:
1.81/1,000 pts



Prevention , why ?

TB Screening Is Effective in Reducing the Risk: EU Experience with Infliximab

TB Reporting Rate per 1000 patients exposed in period



Impact of guidelines on Ois
related deaths ?

Guidelines for Preventing Opportunistic Infections among HIV-Infected Persons—2002

Recommendations of the U.S. Public Health Service and the Infectious Diseases Society of America*

Prepared by Henry Masur, MD; Jonathan E. Kaplan, MD; and King K. Holmes, MD, PhD

Ann Intern Med. 2002;137:435-477.

IDSA GUIDELINES

Summary of the Guidelines for Preventing Opportunistic Infections among Hematopoietic Stem Cell Transplant Recipients

Clare A. Dykewicz

Centers for Disease Control and Prevention, National Center for Infectious Diseases, Division of AIDS, STD, and TB Laboratory Research, Atlanta

Clinical Infectious Diseases 2001; 33:139-44

European evidence-based consensus on the management of opportunistic infections in IBD

1. Definitions
2. HCV, HBV, HIV
3. Herpes virus, HPV, JCV, influenza virus
4. Tuberculosis
5. Parasitic and fungal infections
6. Bacterial infections
7. Specific situations (travel in tropical countries)
8. Work-up before IM therapy - Vaccination

Infections : how to avoid them ?

1. Know the risk factors
2. Primary and secondary prophylaxis
3. Special situation (travel)
4. Food/ lifestyle
5. Vaccination and work up before/during IM

1. Risk factors for developing OI in IBD

- External to the patient
 - geographic clustering
 - Exposure to pathogens
 - Immunomodulator therapy
- Inherent to the patient
 - Age
 - Comorbidity
 - Malnutrition

Serious infections

Logistic Regression Data (Multivariate)

	Odds Ratio	95% CI
Current use of infliximab	0.979	0.619– 1.547
Current use of 6MP/AZA/MTX	0.780	0.507– 1.198
Current use of corticosteroids	2.278	1.478– 3.511*
Current use of narcotic analgesics	2.412	1.560– 3.730*

**p<.001

Risk factors for opportunistic infections in IBD – A case-control study -

	Odds Ratio (95% CI)	P value
Corticosteroid alone	2.2 (1.1-4.8)	0.037
AZA alone	2.5 (1.2-5.1)	0.015
IFX alone	11.2 (0.8-153)	0.07
AZA + CS	15.7 (4.1-59.5)	<0.0001
AZA + IFX	1.6 (0.1-18.7)	0.7
AZA + IFX + CS	Infinite	0.003

1. Risk factors for developing OI in IBD

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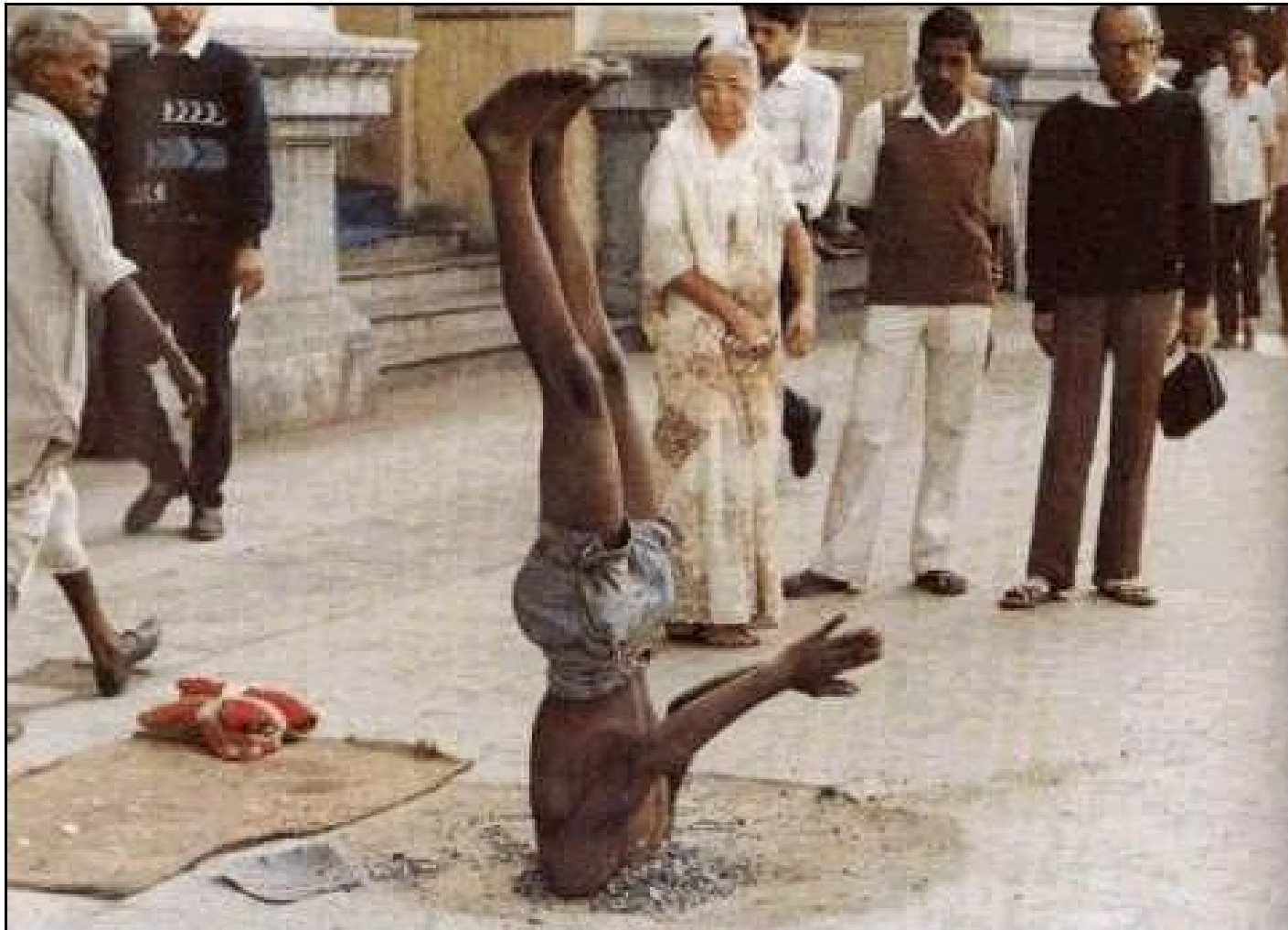
2. Primary and secondary prophylaxis

HBV, HSV, P. Jiroveci, TBC, fungal infection...

ECCO Statement:

No vaccines exist for preventing PCP. For those patients on triple IM with one of these being CsA or IFX, we recommend prophylaxis with co-trimoxazole if tolerated [EL4, RG D]. For those on double IM with one of these being CsA or IFX, a consensus could not be reached on the use of prophylactic co-trimoxazole.

3. Special situation (travel)



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Long term travellers with inflammatory bowel disease **returning from developing countries** should have a **stool examination for bacterial pathogens, ova and parasites** and a complete blood count to identify eosinophilia. For long term travellers with inflammatory bowel disease returning from countries highly endemic for **strongyloidiasis**, serological blood test for strongyloidiasis should be considered [EL5, RG D]

Patients with inflammatory bowel disease should pay greater attention to **precautions regarding food and water** during travel than normal. The immuno-compromised patient should have a low threshold for initiating **self-therapy for traveler's diarrhea with quinolones or azithromycin**, but not rifaximin. If diarrhea does not improve within 48 h despite treatment, medical advice should be sought [EL5, RG D]

3. Special situation (travel)

The risk of Mycobacterium tuberculosis infection in long-term travelers to countries with high-endemicity is of similar magnitude to the average risk of the local population [EL2, R G B]. Patients with inflammatory bowel disease traveling for more than a month to a moderately or highly endemic area should be advised to have a **tuberculin skin test or interferon-gamma release assay (IGRA) before departure**. If negative, it should be repeated approximately **8-10 weeks after returning**. Caution should be exercised in recommending IGRAs, since the predictive value in the immunocompromised is uncertain. Patients with inflammatory bowel disease on immunomodulators should avoid contact with TB patients [EL5, R G D]

4. Food and lifestyle

Salmonella, Listeria, Nocardia, TBC...

Prevention of Salmonella sp. infections consists of **food hygiene** (avoiding raw eggs, unpasteurized milk and insufficiently cooked or raw meat) [EL5, RG D]

Prevention of Listeria sp. infections includes **avoidance of unpasteurized milk or cheese, uncooked meat and raw vegetables**, especially during pregnancy [EL5, RG D]. Patients on anti-TNF therapy who present with meningitis or other neurological symptoms demand full attention and should be thoroughly investigated as soon as such symptoms develop [EL5, RG D]

Prevention of Nocardia sp. infections consists of **avoiding direct contact with soil or inhalation of soil contaminated dust**. [EL5, RG D]

Vaccination and systematic work-up to consider before/during IM therapy

- Detailed interview
- Physical examination
- Laboratory tests
- Screening for tuberculosis
- Vaccination

Detailed interview

- History of bacterial infections
- History of fungal infections
- Risk of latent or active tuberculosis:
 - date of the last BCG vaccination
 - potential contact with patients having TB
 - country of origin, or prolonged stay in an area endemic for TB
 - history of treatment for latent or active TB
- History of varicella-zoster virus infection (chickenpox/shingles)
- History of herpes simplex virus infection
- Immunization status for hepatitis B
- History of travel and/or living in tropical area or countries with endemic infections
- Future plans to travel abroad to endemic areas

Physical examination

- Systemic or local signs of active infection
- Cervical smear

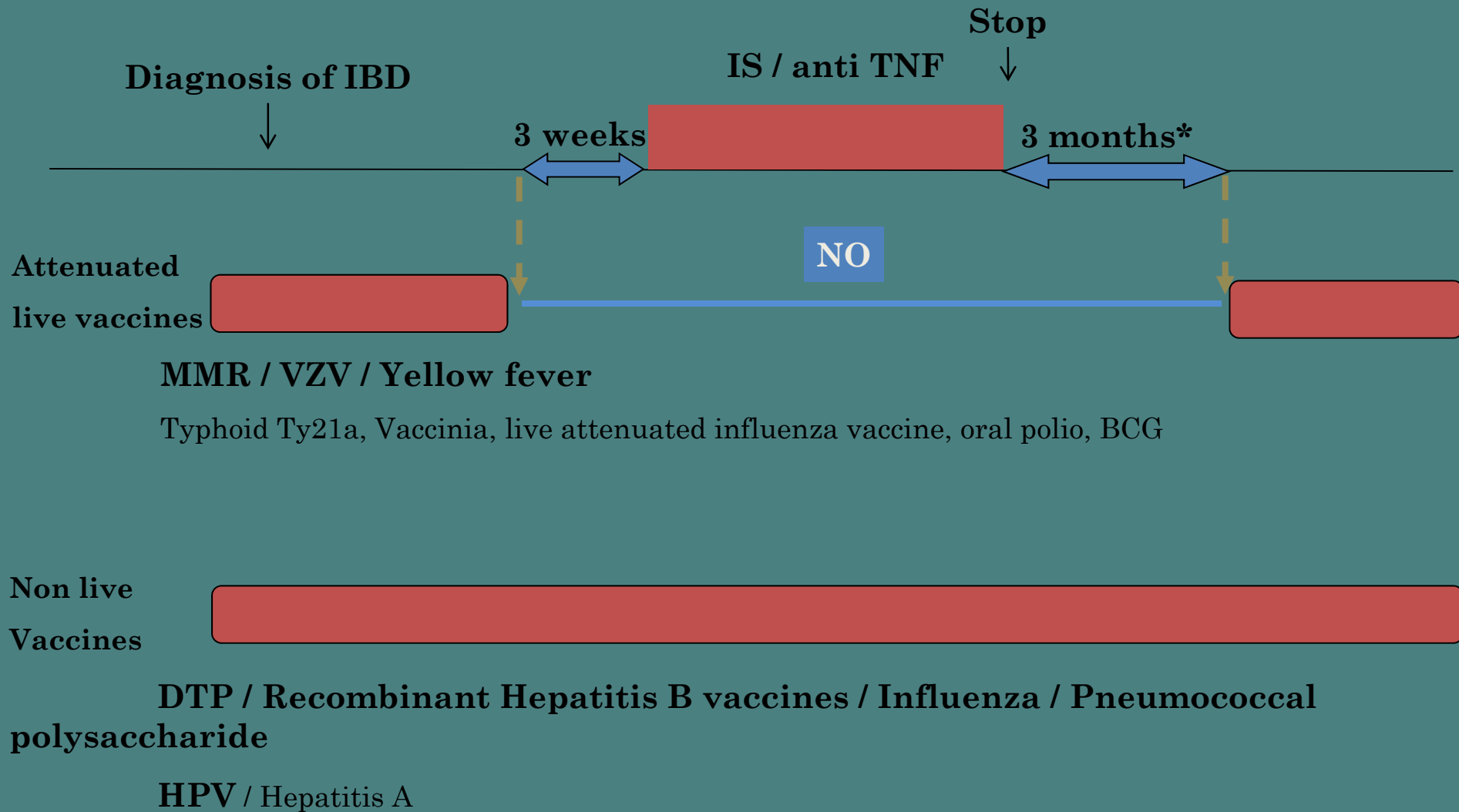
SCREENING FOR TUBERCULOSIS

- According to national guidelines

Laboratory tests

- Neutrophil and lymphocyte cell count
- C-reactive protein
- Urine analysis in patients with prior history of urinary tract infection or urinary symptoms
- Varicella zoster virus (VZV) serology in patients without a reliable history of varicella immunization
- Hepatitis B virus (HBV) serology
- Human immunodeficiency virus (HIV) serology
- Eosinophil cell count, stool examination and strongyloidiasis serology (travel in developing countries)

Vaccines in IBD patients



* This delay may be reduced to 1 month in case of use of corticosteroids alone

Vaccination in practice

- Best before introduction of immunomodulator therapy.
- Immunization status of patients with IBD should be checked and vaccination considered for routinely administered vaccines: tetanus, diphtheria, poliomyelitis, pertussis.
- Every patient with IBD should be considered for the 5 following vaccines:
 - VZV varicella vaccine (if there is no medical history of chickenpox, shingles, or VZV vaccination and VZV serology is negative)
 - Human papilloma virus
 - Influenza (trivalent inactivated vaccine) once a year
 - Pneumococcal polysaccharide vaccine (single booster 3-5 years)
 - Hepatitis B vaccine in all HBV seronegative patients
- Vaccines for patients on immunomodulators traveling in developing countries or frequently traveling around the world should be discussed with an appropriate specialist.

Identification du patient

Coller ici l'étiquette du patient ou inscrire son nom, sa date de naissance ou toute autre information qui permette de l'identifier

Maladies Inflammatoires Chroniques Intestinales (MICI)

Check-list pour la prévention des infections lors de traitement
À conserver dans le dossier médical de chaque patient



La réunion de Consensus de l'ECCO sur les infections opportunistes chez les patients MICI a réuni 30 gastroentérologues et spécialistes des maladies infectieuses. Elle a permis l'élaboration de recommandations européennes sur la prise en charge et la prévention des infections, qu'elles soient opportunistes ou non, chez ces patients.

Cette check-list a pour objectif de fournir à chaque gastroentérologue l'ensemble des items qui, selon ces recommandations, sont à prendre en compte avant et pendant un traitement immunomodulateur. Idéalement, cette check-list sera remplie lors de la première visite, et si possible avant de débiter un traitement immunomodulateur. La check-list pourra être complétée lors des visites ultérieures.

1. Interrogatoire du patient

Historique de maladie infectieuse

Bactérienne

OUI NON Date : ____/____/____

Historique :

Fongique

OUI NON Date : ____/____/____

Historique :

Virale

Herpes simplex (boutons de fièvre ou génitaux)

OUI NON Date : ____/____/____

Historique :

Varicelle ou Zona

OUI NON Date : ____/____/____

Historique :

Autre

OUI NON Date : ____/____/____

Historique :

Parasitaire

OUI NON Date : ____/____/____

Historique :

Autres infections

Séjour prolongé (voyage ou lieu de résidence) dans un pays tropical ou une zone d'endémie

OUI NON Date : ____/____/____

Historique :

Projets de voyage dans un pays tropical ou dans une zone d'endémie

OUI NON Date : ____/____/____

Historique :

Commentaires :
.....
.....

2. Examen physique : n'oubliez pas d'interroger le patient et de rechercher des signes d'infection active

Commentaires :
.....
.....

3. Tests de dépistage de la tuberculose

Radiographie pulmonaire

Teach your patient

Know your patient

Examine your patient

Screen your patient

Treat your patient

Monitor your patient (keep a close link)