

Current Topics in General Medicine

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Movie hero who believes his wife was poisoned by an MRI scan



Agonising condition: Film star Chuck Norris and his wife Gena

I started to treat myself,' she says. 'I'd read that gadolinium can damage the mitochondria "powerhouse" in cells, restricting the energy that enters cells, so I increased the amount of antioxidant foods I ate, eating lots of fresh vegetables. This was to counter the free radical damage. 'I also took supplements such as co-enzyme Q10, which can improve energy release. A year on, Catmona's symptoms



SHOWBIZ MINUTE

NORRIS SUES OVER MRI CHEMICAL



Chuck Norris claims his wife was poisoned during MRI scans, sues for \$10 million

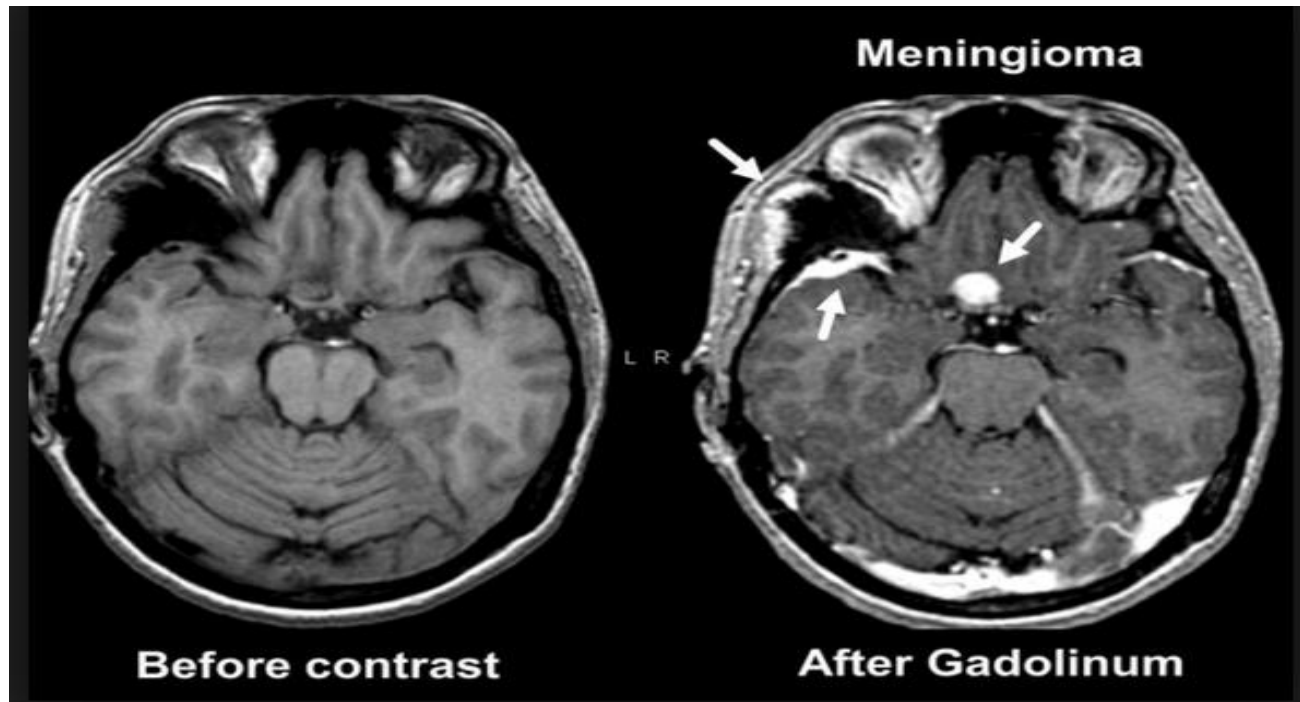
By Lindsey Bever November 8

The Washington Post
Democracy Dies in Darkness



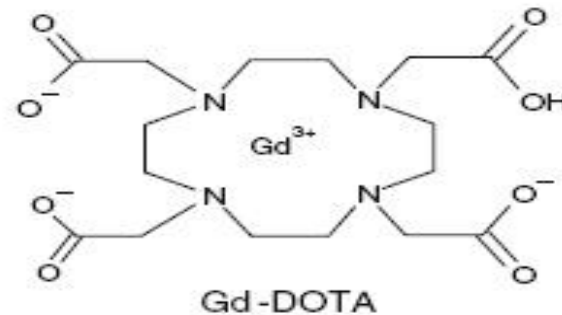
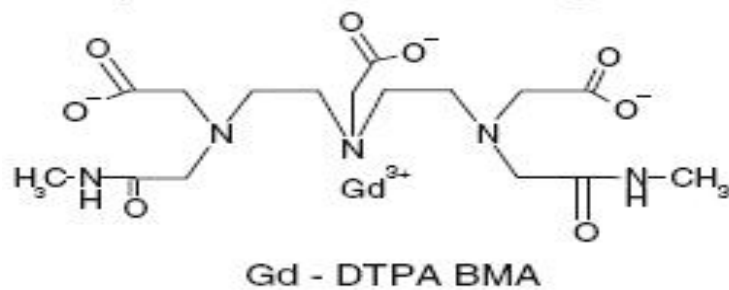
MRI

- 30 million scans performed per year
- 30% using gadolinium based contrast agents (GBCA)
- Excellent safety profile- hypersensitivity reactions <0.01%



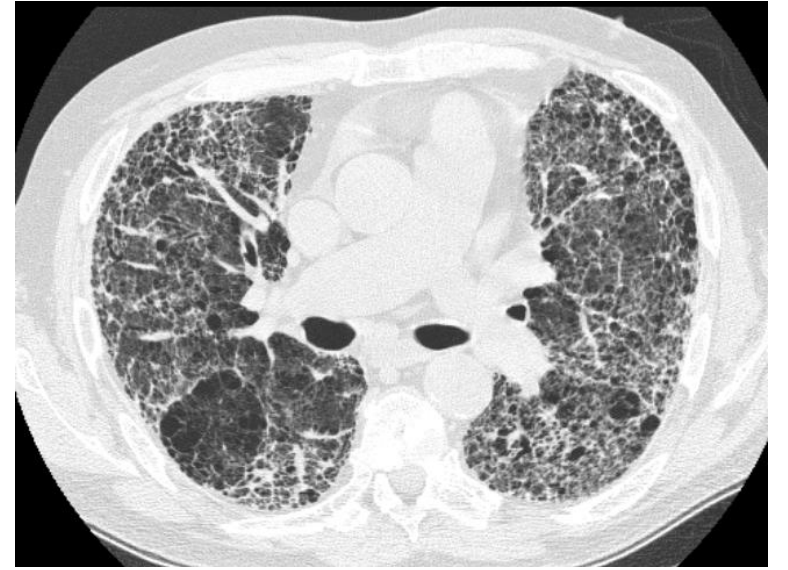
Gadolinium

- Used since late 1980s to enhance MRI
- Free Gd^{3+} similar size to Ca^{2+} = TOXICITY
- Therefore bound to chelating ligands
 - Linear- 2-20% dissociation*
 - Macrocyclic- much more stable
- Widely distributed across tissues
- Predominantly renally cleared $t^{1/2} = 1-3$ hrs



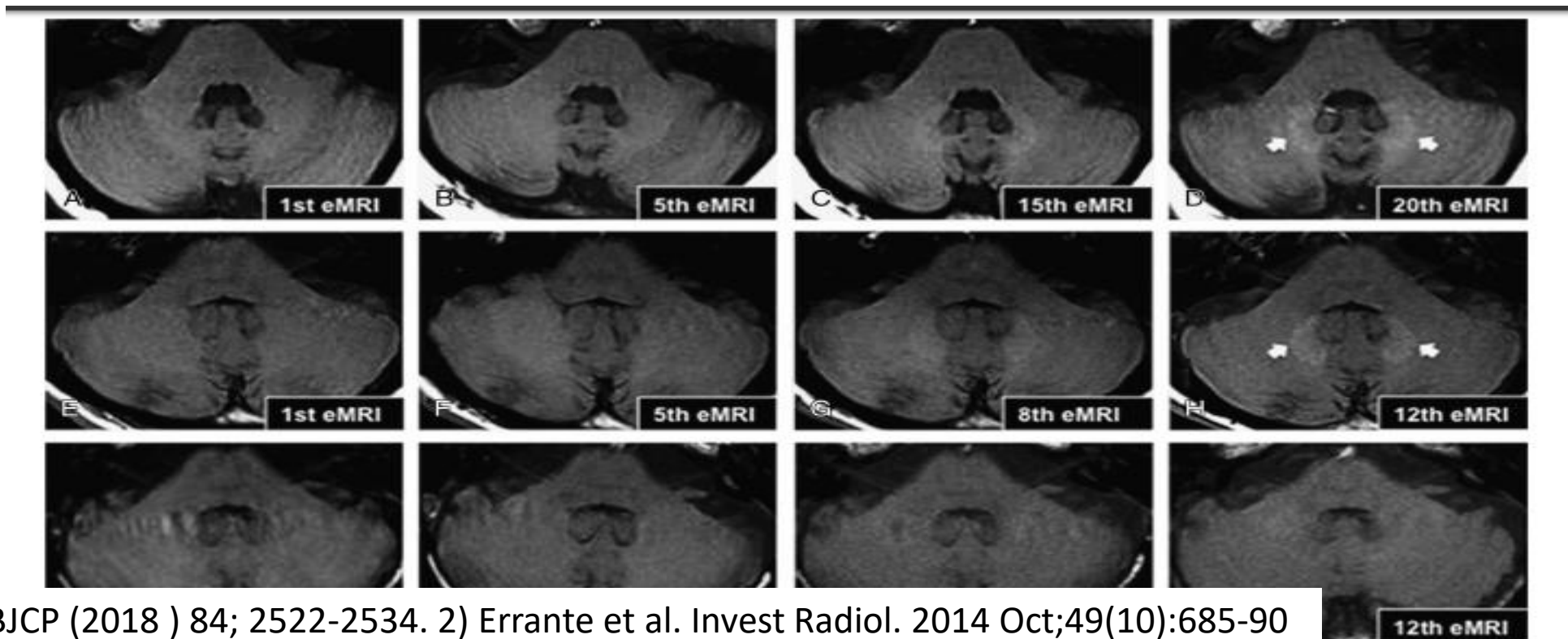
Nephrogenic systemic fibrosis

- Identified 2006
- End stage renal failure
- Linear contrast agents
- ?due to reduced clearance
- Now very rare



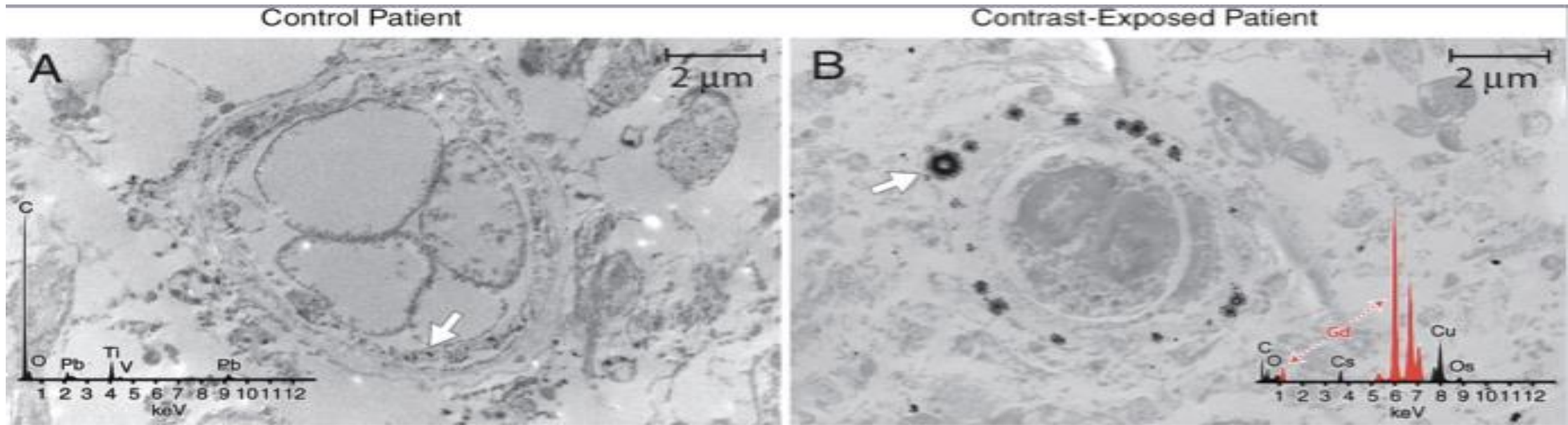
Evidence for accumulation of gadolinium

- Mid 2000's evidence of gadolinium deposition in femoral head¹
- 2014 brain- progressive increase T1 signal in dentate nucleus²



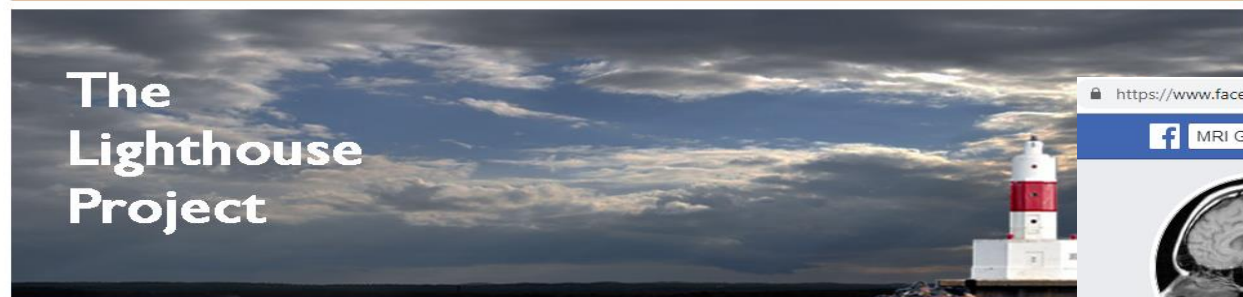
More evidence of gadolinium accumulation

- Post mortem study gadolinium deposits seen on electron microscopy and mass spectrometry in dentate nucleus and globus pallidus



Gadolinium Toxicity

shedding light on the effects of retained gadolinium from Contrast MRI

The Lighthouse Project

Welcome

We started the Lighthouse Project to shed light on the effects of retained Gadolinium from Gadolinium-Based Contrast Agents (GBCAs) used for contrast-enhanced MRIs and MRAs. This website is part of our effort to increase awareness of the effects of Gadolinium Toxicity.

GBCAs are generally thought to be safe to use in patients with good kidney

VIEWPOINTS
Ideas from c
related to G

VIEWPOINT C
...

WEBSITE PAGES

Background

NSF



MRI Gadolinium Toxicity
@gadoliniumtoxicity

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MRI-Gadolinium-ToXicity

Restricted Group, 813 members

Conversations Photos Files About More



Gadolinium Deposition Disease?

- Proposed after surveys of online forums with a self diagnosis of gadolinium toxicity
- Brain fog, burning of skin, pain of bones or joints, muscle vibration, head pain, skin pain or thickening
- Offer chelation therapy to bind gadolinium
- Risk of electrolyte / trace element depletion – can be fatal
- American College of Medical Toxicology - position statement
 - Not scientifically validated, no benefit, may be harmful

Current recommendations

- July 2017 – EMA:
 - EU-wide suspension of all commercially available linear GBCAs
 - Apart from gadoxetate and gadobenate dimeglumine taken up in the liver and “meet an important diagnostic need”
- December 2017 – MHRA and FDA:
 - Minimise requests for GBCA-enhanced MRI unless essential
 - MHRA suspended licencing for linear agents, gadodiamide (Omniscan) and intravenous gadopentetic acid (Magnevist)
 - MHRA advise the use of gadoxetate and gadobenate dimeglumine be limited to liver imaging

Where are we now?

- Gadolinium based contrast agents are essential components of MRI to allow accurate diagnosis with excellent safety profile
- Risk of neural gadolinium deposition with **all agents** but greater with linear agents – many recently removed from clinical practice
 - Patients with infective, inflammatory or malignant disease
- Further work needed to establish to determine whether gadolinium deposition is associated with clinically significant sequelae
- Normal ranges for those not exposed to GBCA

POOPED Poo donors wanted as demand for faecal transplants soars and donation banks run dry

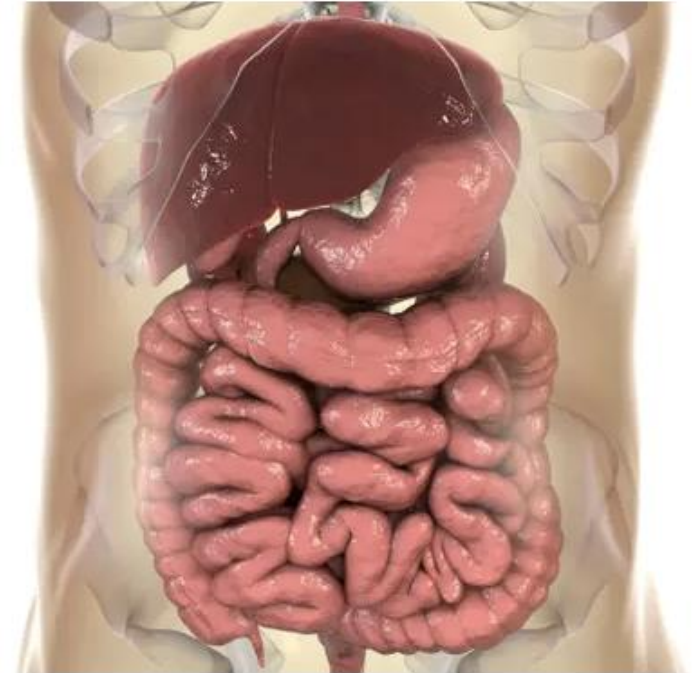
Gemma Mullin, Digital Health Reporter

19 Jun 2019, 10:27 | Updated: 19 Jun 2019, 10:27



Faecal transplant researchers identify 'super-pooper' donors

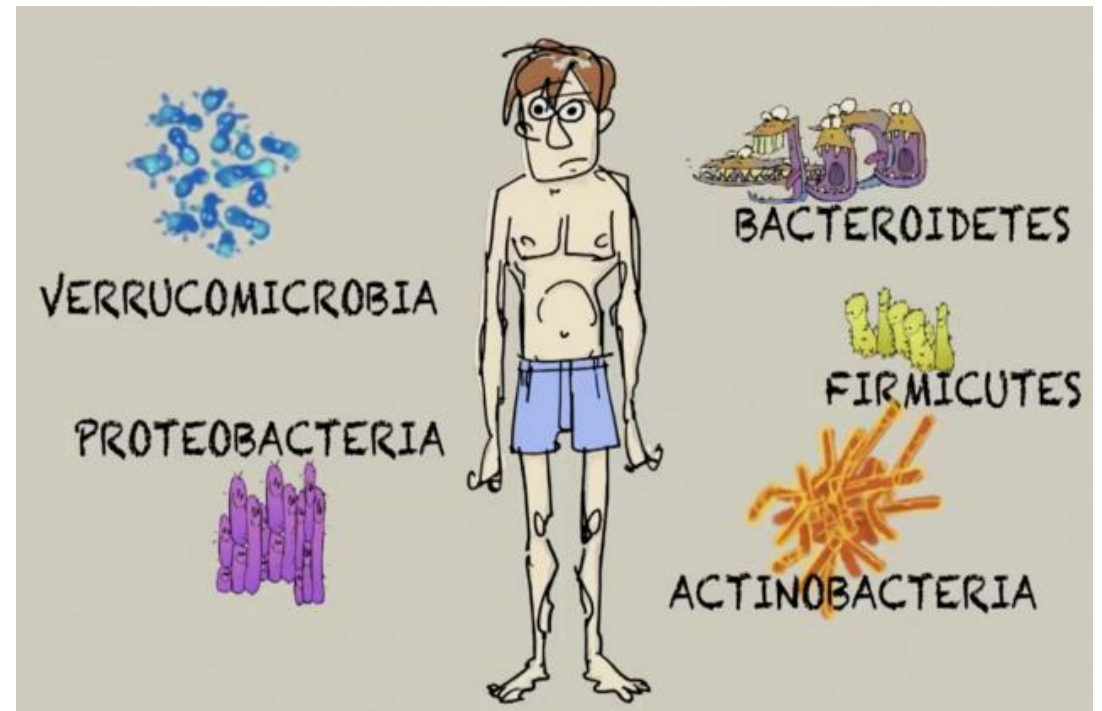
Study finds stool transplants from some donors are far more effective than others



▲ Illustration of the digestive system Photograph: Science Photo Library/Alamy

Gut microbiome

- Human gut has diverse population of microbes
- 1kg or 37 trillion bacteria, 500-1000 species in human gut
- Key roles in
 - Nutrition
 - Energy metabolism
 - Immune development
 - Host defence
- Genetic factors v Environmental
 - Diet
 - Stress, exercise
 - Immune system



Altered microbiota (low diversity) = dysbiosis

- Negative functional outcomes in physiology
 - Inflammation
 - Disturbed metabolic processing
- Conditions associated
 - *C. Difficile* infection
 - Obesity
 - Allergic disease
 - Inflammatory bowel disease
 - Irritable bowel syndrome

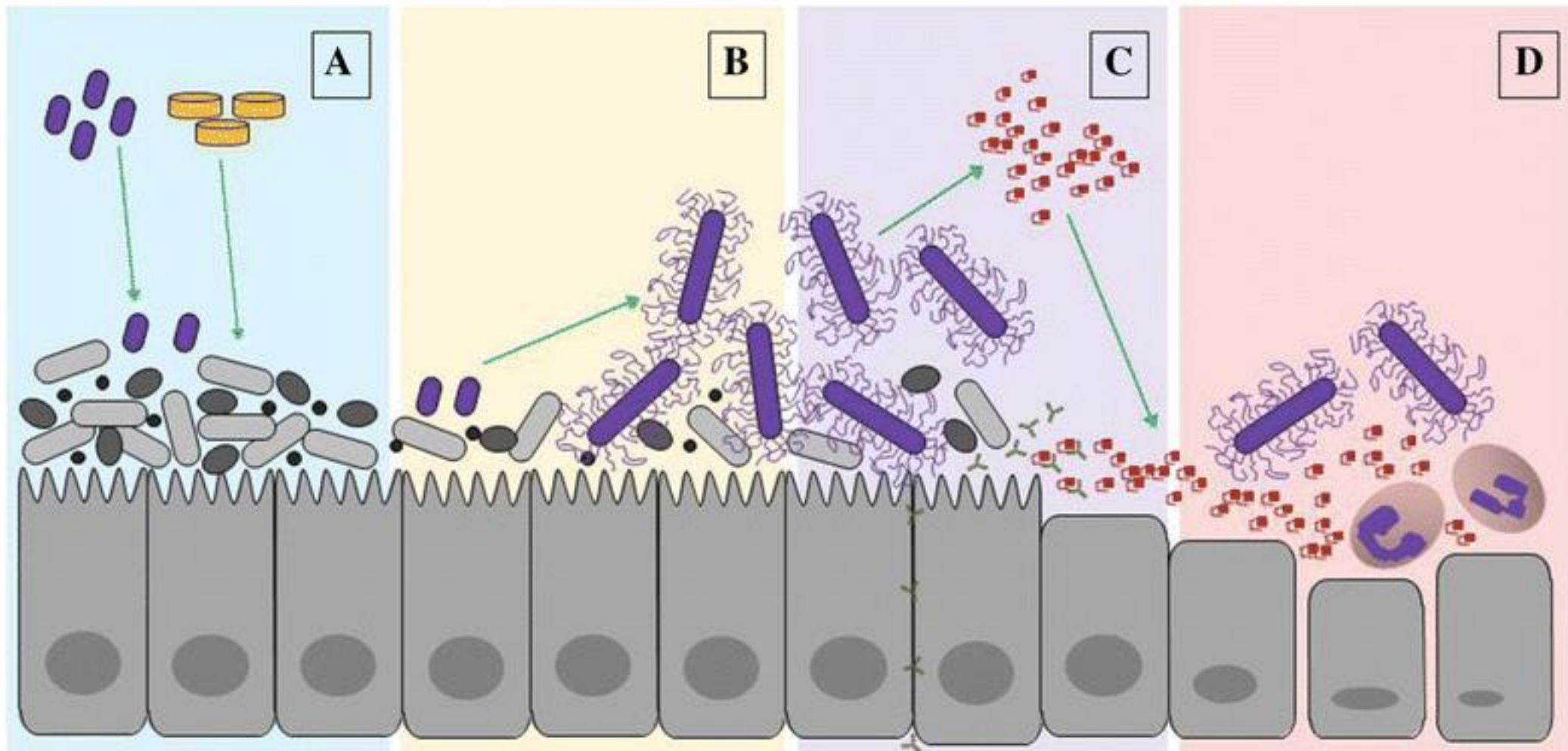
Faecal Microbiota Transplant (FMT)

- China in 4th century to treat poisoning and diarrhoea
- Used in veterinary medicine in cows in 17th century
- Over the last 30 years rising epidemic of virulent *C. Difficile* infection and greater understanding of gut microbiome

Clostridium Difficile

- Opportunistic gut pathogen suppressed in healthy individuals by commensal organisms
- When gut microbial diversity is reduced e.g after antibiotics
- Can proliferate producing enterotoxins causing inflammation and diarrhoea
- First line treatment is with antibiotics- cure rate 80%
- 20% develop recurrence

- antibiotics
- C. difficile* spores
- vegetative *C. difficile*
- C. difficile* toxins
- enterocytes
- normal gut microbiota
- lymphocytes
- neutrophils



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Duodenal Infusion of Donor Feces for Recurrent
Clostridium difficile

Els van Nood, M.D., Anne Vrieze, M.D., Max Nieuwdorp, M.D., Ph.D., Susana Fuentes, Ph.D.,
Erwin G. Zoetendal, Ph.D., Willem M. de Vos, Ph.D., Caroline E. Visser, M.D., Ph.D., Ed J. Kuijper, M.D., Ph.D.,
Joep F.W.M. Bartelsman, M.D., Jan G.P. Tijssen, Ph.D., Peter Speelman, M.D., Ph.D.,
Marcel G.W. Dijkgraaf, Ph.D., and Josbert J. Keller, M.D., Ph.D.

Donor selection

- Partner or spouse- Shared environment
- First degree relative- Similar genetics and immune responses
- Unrelated
- All screened
 - **Serology:** Hep A/B/C, HIV, syphilis
 - **Stool:** *C. Difficile* toxin, culture and OCP
 - Consider viruses, E. Coli 0157, cryptosporidium and giardia
 - Possibly CMV, EBV, HTLV, H.pylori, schistosomiasis, MRSA, VRE

Stool preparation/administration

- Homogenise in blender- water, milk or sterile saline
- Filtered through gauze or coffee filter
- Formed in capsules and coated in gelatin
 - May be frozen and thawed later
- Infused into GI tract
 - Endoscopic UGI, LGI
 - Nasogastric tube – risk of aspiration
 - Enema

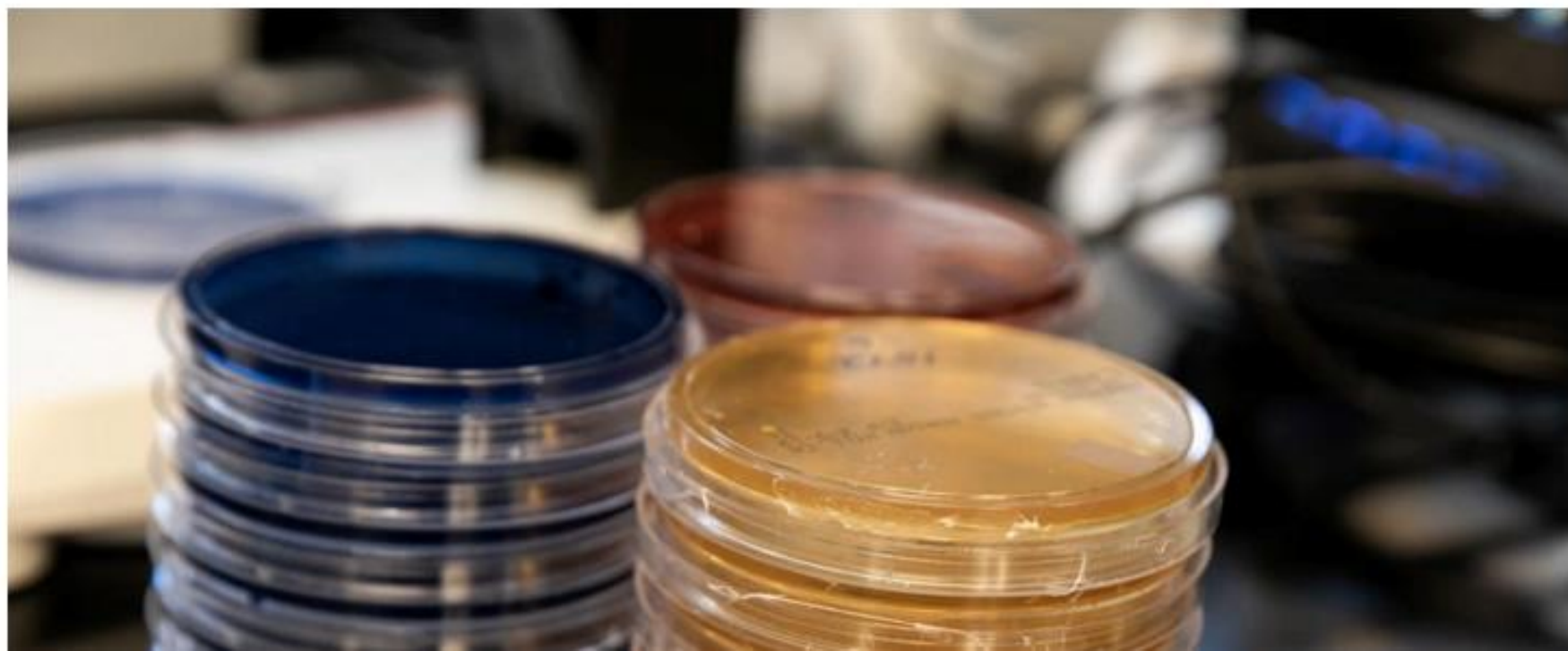


After the event

- Microbiome studies show FMT last from days to years
 - Gradual switch back to baseline population of microbes
 - Diet, antibiotics use, disease process, immune status
- Not a problem for *C. Difficile* as restored commensals prevent growth
- Crohn's and Ulcerative colitis
- Studies shown specific stool donors can have better response
- **Super-donors**
 - Difficult to predict
 - Another approach is pooling of stool

Fecal Transplant Is Linked to a Patient's Death, the F.D.A. Warns

The agency said two patients received donated stool that had not been screened for drug-resistant germs, leading it to halt clinical trials until researchers prove proper testing procedures are in place.



Summary

- Growing acceptance Faecal Microbiota Transplant to treat *C. Difficile*
- Role in other diseases related to gut dybiosis less clear at present
- Super-donors may become clearer for specific conditions
- Need to ensure robust screening procedures

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ANALYSIS
Fungus is the next 'superbug' to threaten human health

By Justin Beardsley
Updated 16 Apr 2019, 9:11pm



Mail Online

The deadly spores that could be hiding in your home or garden: Experts warn of 'serious and immediate' threat posed by drug-resistant fungi that can cause lung disease



EXPRESS

Home of the Daily and Sunday Express

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TIRED? Blame this accidentally released SUPER-FUNGUS which is now in YOUR garden

BRITISH farmers are being blamed for accidentally creating of drug resistant SUPER-FUNGUS which can infect the lungs and bloodstream and are springing up in gardens across the country.

FINANCE **TRAVEL**
SUNDAY SCOTLAND

THE SUNDAY TIMES

r 8, 20

Just register a few details

Compost heaps help spread killer superfungi



Drug-resistant fungi are appearing in gardens and compost heaps

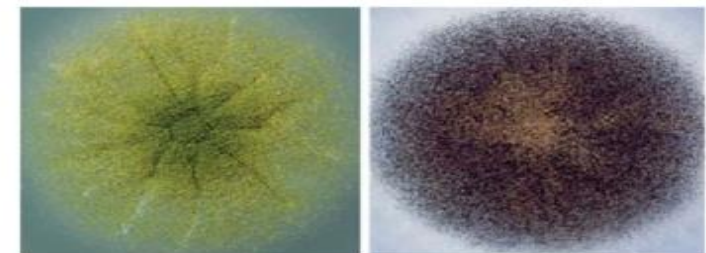
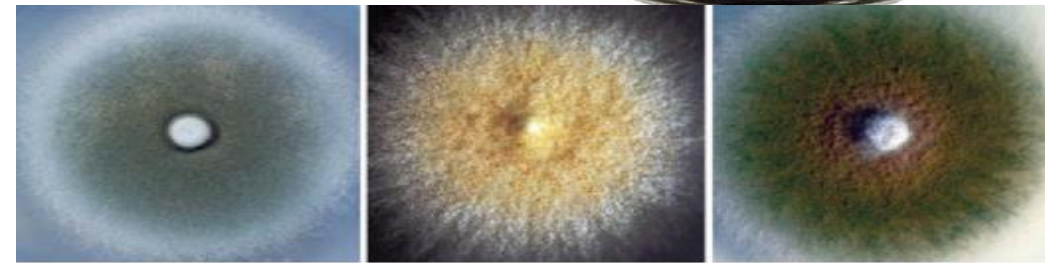
Aspergillus

- Ubiquitous, saprophytic fungi
- Found in soil or decaying vegetation
 - Significant role in carbon and nitrogen recycling

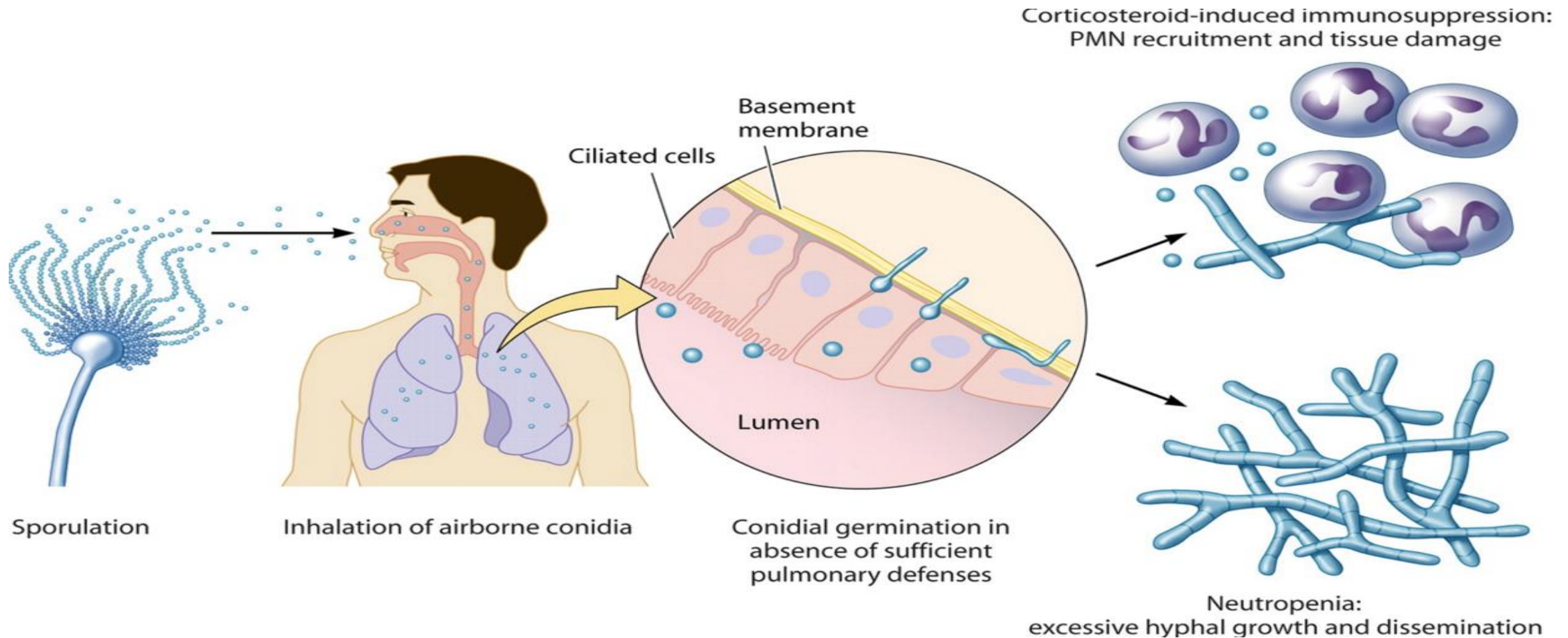


Aspergillus species

- Genus *Aspergillus* ~ 200 species
- **Rich enzymatic profile**
 - *A. terreus*: lovastatin
 - *A. oryzae*: soya bean = soy sauce, rice = sake
 - *A. niger*: citric acid, amylase and proteases
- **~ 20 pathogenic in humans**
 - *A. fumigatus*
 - *A. flavus* - aflatoxin - HCC
 - *A. niger*
 - *A. nidulans*

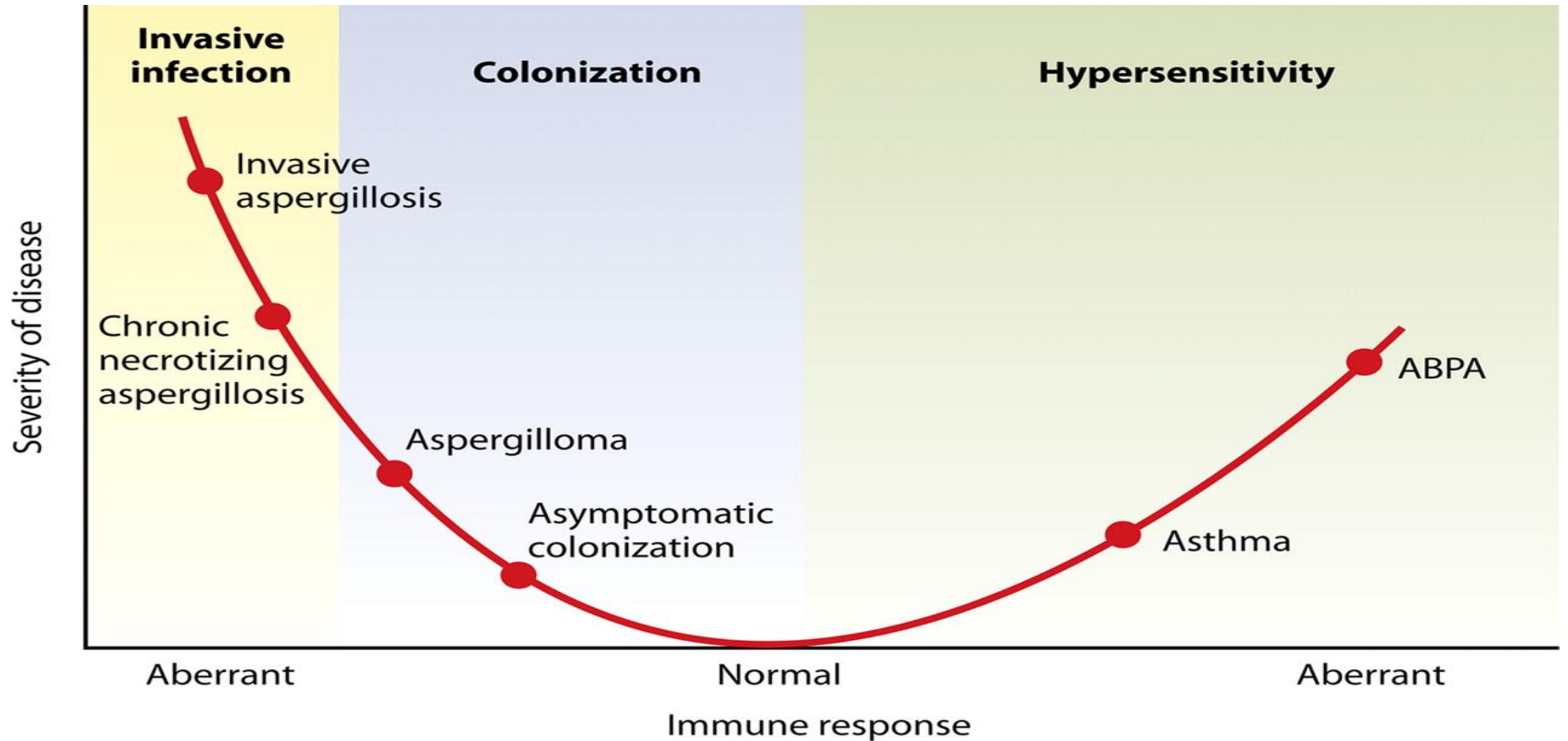


Infection with *Aspergillus Fumigatus*

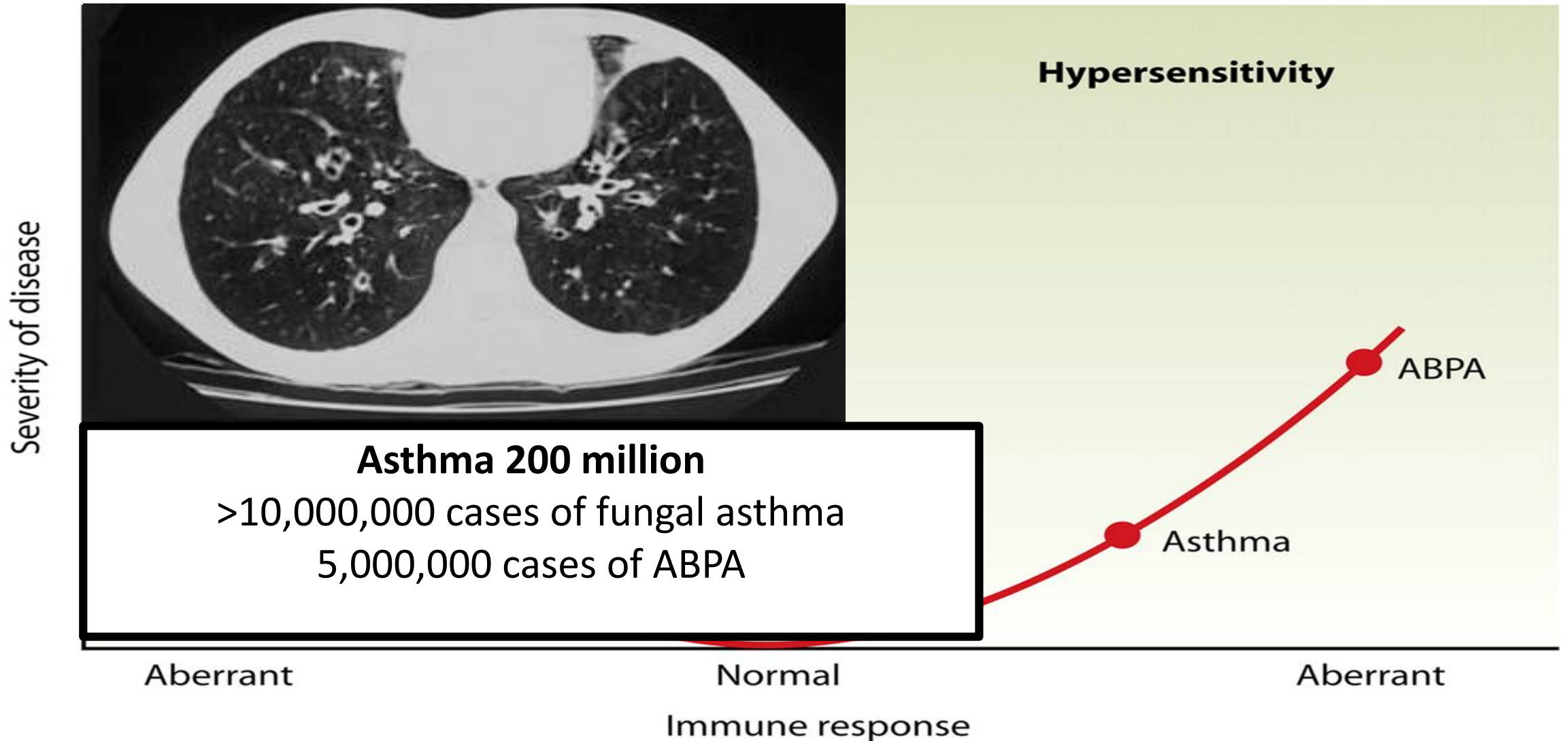


1,000 spores per day

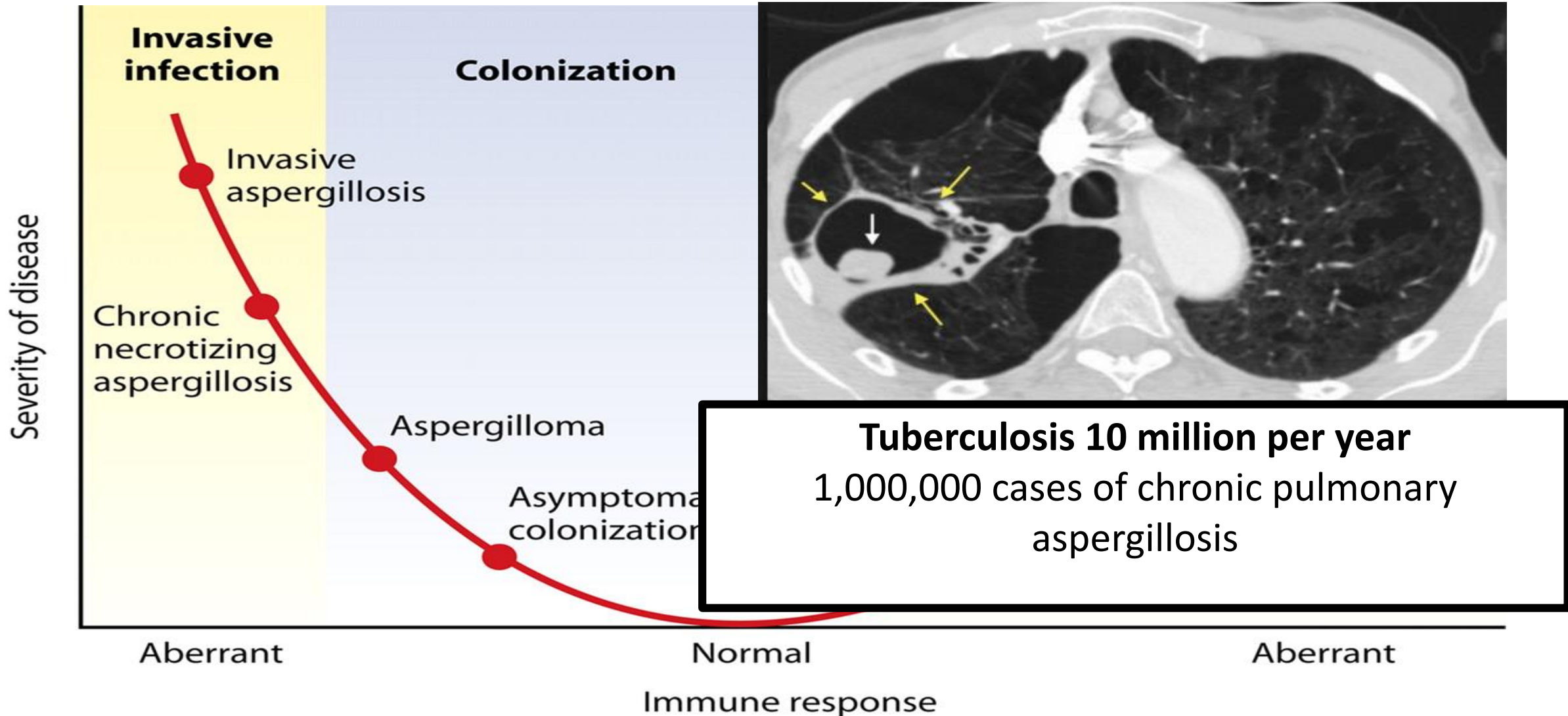
Immune response in aspergillosis



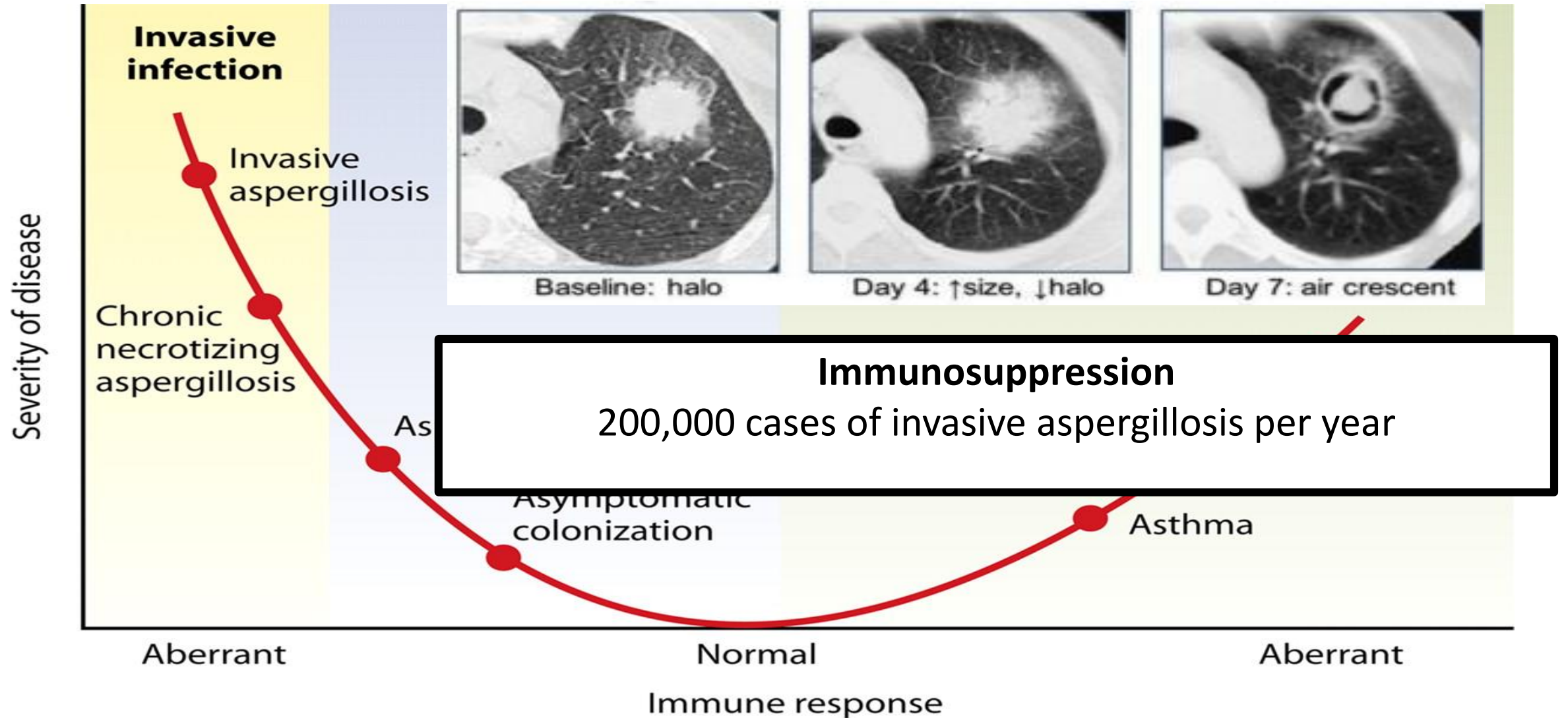
Immune response in aspergillosis



Immune response in aspergillosis



Immune response in aspergillosis



Drugs with anti-aspergillus activity

- **Triazole**

- Itraconazole, Voriconazole, Posaconazole

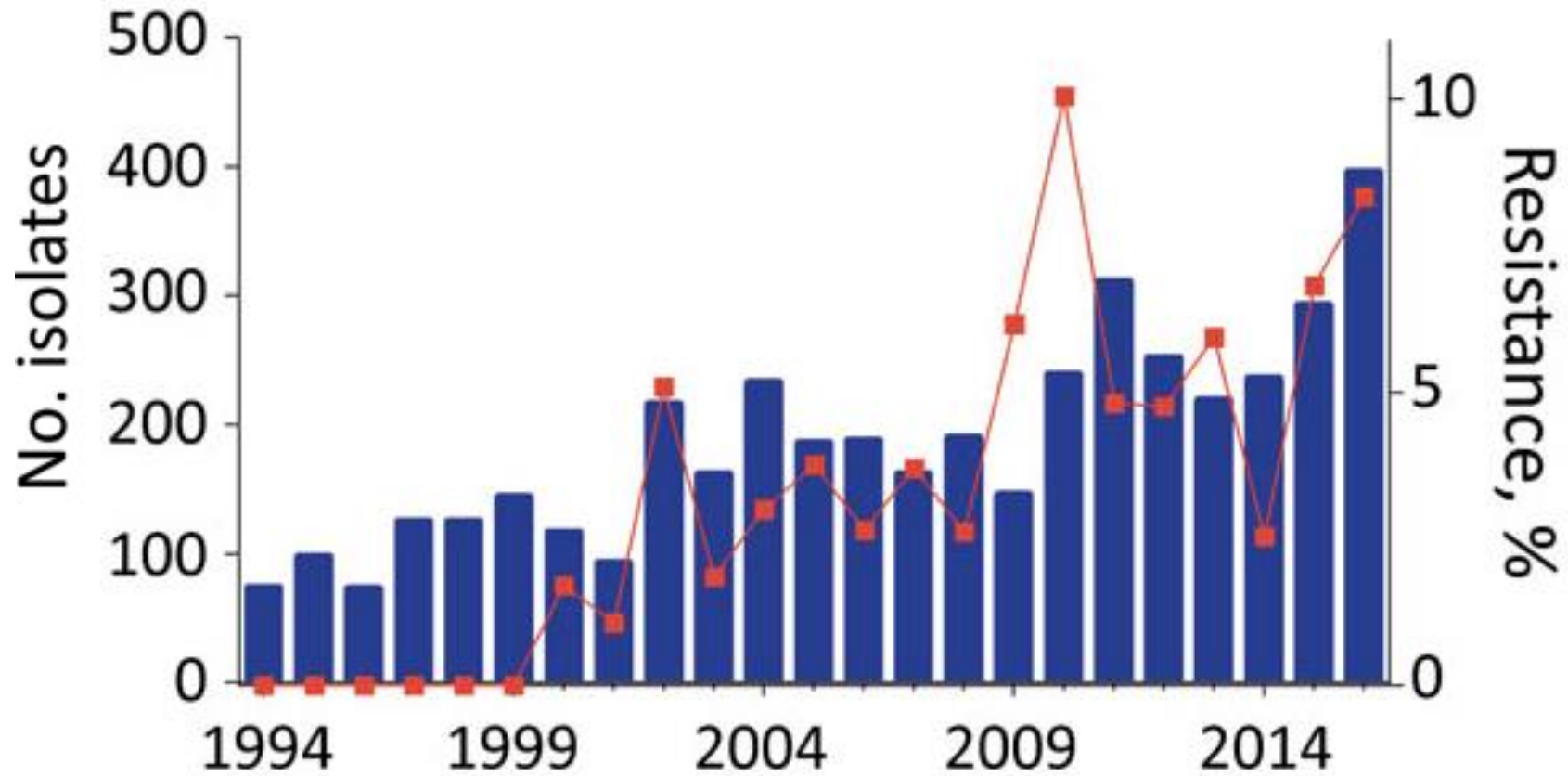
- **Polyene**

- Ambisome

- **Echinocandins**

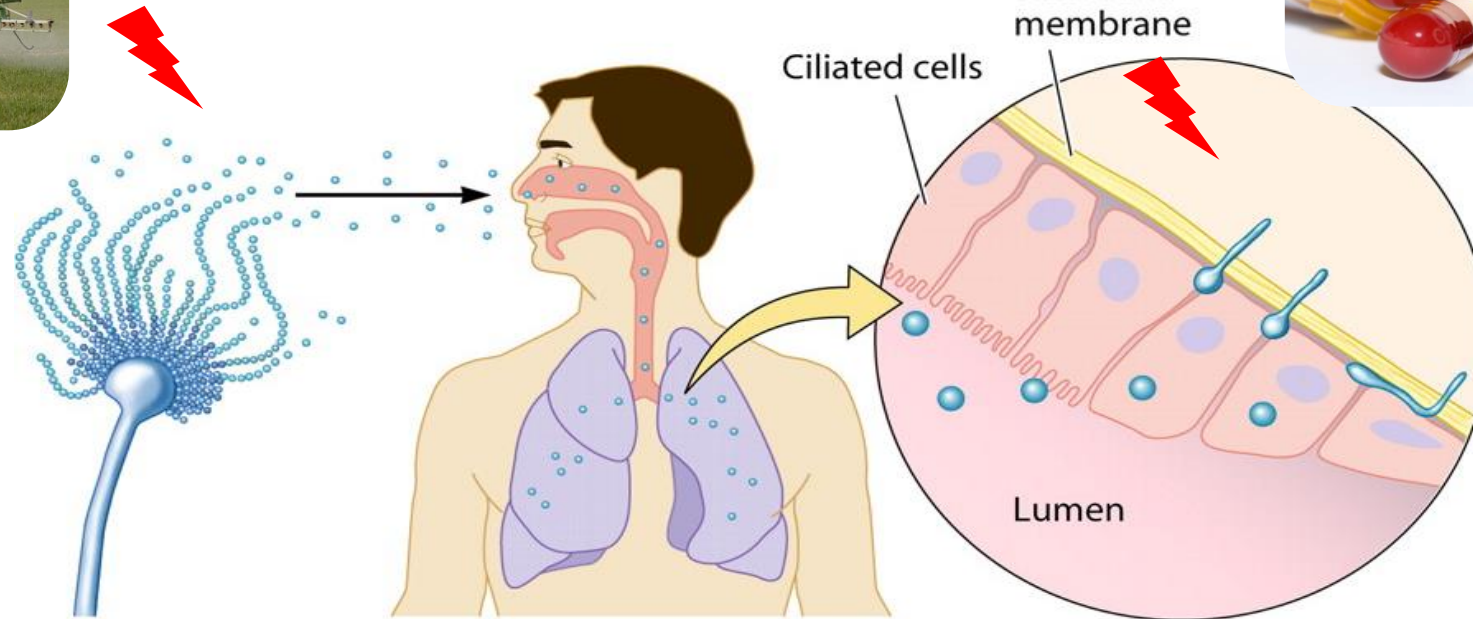
- Caspofungin, Anidulafungin, Micafungin

Increase in azole resistant *A. fumigatus* 1994-2016, Nijmegen

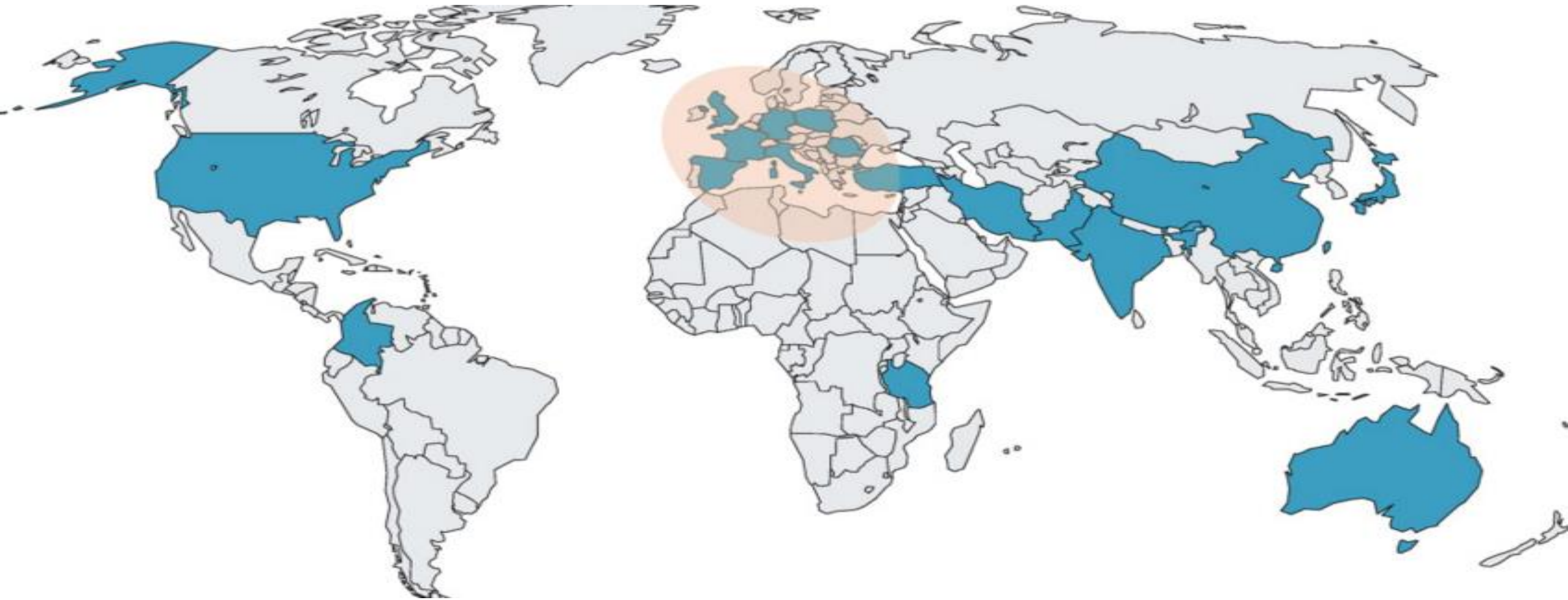


- Passive surveillance 2014-2016 in London cardiothoracic centre showed 13% (22/167) resistance

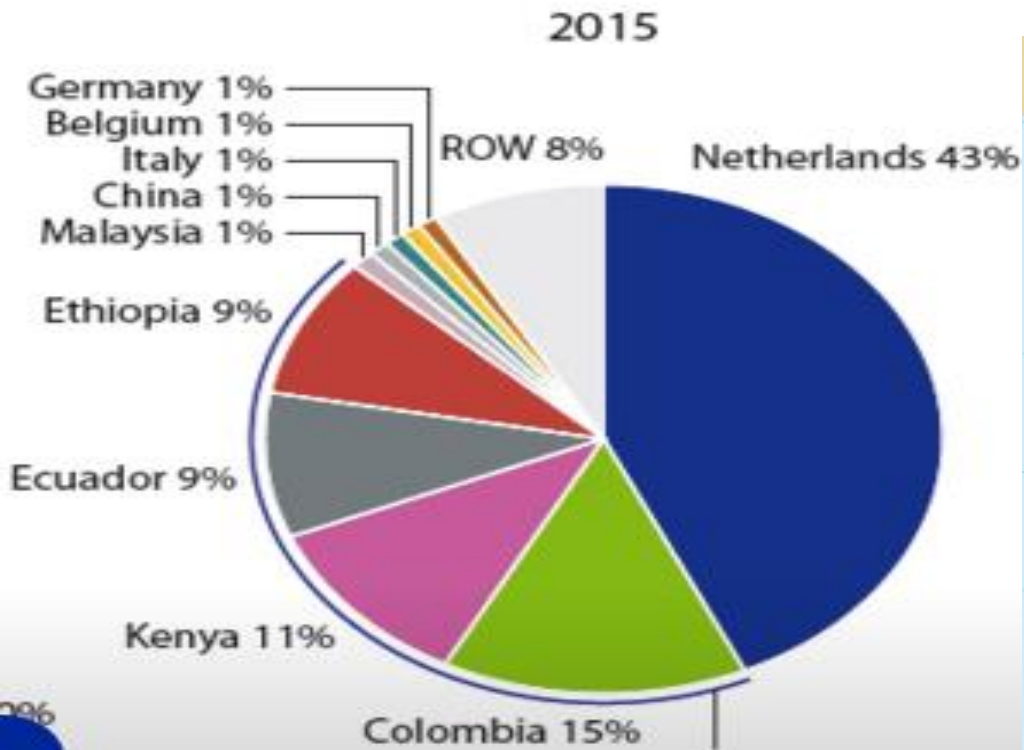
Mechanisms of azole resistant *A. fumigatus*



Global burden of azole resistant *A. Fumigatus*



Flower industry



World's largest cut flower exporters 2015



Trade of flower bulbs, cut flowers, cut foliage and living plants 2016

Key points

- Spectrum of disease caused by *A. Fumigatus* related to host immune response
- Emergence of azole resistance – with cross resistance
 - Medical or Environmental

Study links hot drinks to cancer: What to know about your coffee and tea

Brett Molina and Ashley May | USA TODAY
Published 6:06 AM EDT Mar 28, 2019

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**Put milk in your tea to fight off cancer:
Drinking piping hot tea or coffee could
'double your risk of developing
tumours in the oesophagus'**

Hot drinks and cancer

- Several studies shown ↑ risk oesophageal cancer and hot drinks
 - 3x retrospective- recall bias
 - 3x prospective- self-reported perception of temp.
- International Agency for Research on Cancer listed drinking very hot drinks as a **probable carcinogen**
- Proposed mechanism
 - Thermal injury leading to inflammation
 - Impaired barrier function leads to intraluminal exposure of other carcinogens
 - Ingredient in beverage

Published this year

- Prospective study in Golestan Province in Iran
- High rates of SCC of oesophagus
 - 50,000 people, 10 years median follow up, 40-75 yrs
- Measured temperature of tea at baseline as well as subjective preference for hot tea drinking and time from pouring to drinking
- Annual follow up
- Questionnaire on
 - Standard of living, smoking, chewing tobacco, opium, alcohol
- Review of death and cancer registries

After correcting for confounders

- **Measured tea temperature**, reported **preference for very hot tea** and **shorter time to pouring** all associated with \uparrow risk
- 700ml black tea at temp $>60^{\circ}\text{C}$
- 1.9x times risk of squamous cell oesophageal carcinoma



As you may not have thermometer in work....

- If you can hold your mug tight for 20 seconds – the contents should be less than 60 C



Acknowledgments

- Kerry Layne, GSTT
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- Darius Armstrong-James, Imperial College
- Laura Waters, Mortimer Market Centre

- Any questions?