

# The year 2013

## A subjective selection



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# The year in neurological infections



# 1. New pathophysiological features

## **Herpes Simplex Virus Encephalitis is a Trigger of Brain Autoimmunity**

T. Armangue et al. Ann. Neurol. 2014, 75 (2): 317-23

- Five prospectively diagnosed patients with relapsing post-herpes simplex encephalitis.
- Retrospective assessment of 34 HSE-patients
- Detection of anti-NMDAr antibodies in serum and CSF

# Results

- In the 5 prospective cases:
  - Identification of anti-NMDAr-Abs in all cases
  - Antibodies synthesis started 1-4 weeks post-HSE, preceding the neurological relapse.
- Among the 34 retrospective cases:
  - 2 with anti-NMDAr-Abs,
  - 9 with unknown neuronal surface-antibodies
  - 1 with NMDAr and unknown antibodies

# Treatments and outcome

- 1 patient improved spontaneously
- 4 patients received immunotherapy
  - 1 improved with steroids
  - 3 did not improve with steroids and IVIg
    - Switched to rituximab (375mg/kg, weekly, 4 weeks) and cyclophosphamide (monthly IV pulses, first dose: 500 mg/m<sup>2</sup>, subsequent doses: 750 mg/m<sup>2</sup>)
    - **cured or improving at the time of evaluation**

# Comments

- Relapsing post-HSE might often be anti-NMDAR encephalitis !!!
- Immune response underlies different complications (e.g., choreoathetosis in children, abnormal behavior in adults), which may occur in contiguity or a few weeks after HSE
- HSE is a trigger of cell-surface/synaptic autoimmunity. ***What about other viruses ?????***

# The future?

- Patients with prolonged, worsening or relapsing symptoms post-HSE should be tested for anti-NMDAr and other anti-synaptic receptors Abs
- Anti-NMDAr Abs-related symptoms are responsive to immunotherapy in most cases
- Immunotherapy appears to be safe in patients with relapsing symptoms post-HSE



**The causative pathogen determines the inflammatory profile in CSF and outcome in patients with bacterial meningitis**

D. Grandgirard et al.

Mediators of inflammation, 2013. doi: 10.1155/2013/312476

- Comparison of inflammatory CSF profile in patients with meningitis due to *S. pneumoniae*, *H. influenzae* or *N. meningitidis*
- *S. pneumoniae* meningitis had higher concentrations of cytokines, IFN-gamma and matrix-metalloproteinase-9
- Case fatality rate was 46% in case of *S. pneumoniae*, 27% in case of *N. meningitidis* and null in case of *H. influenzae*

**The causative pathogen determines the inflammatory profile in CSF and outcome in patients with bacterial meningitis**

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Mediators of inflammation, **2013**. doi: 10.1155/2013/312476

- Significant association between death and CSF levels of IL-1beta, TNF-alpha, IL -1RA, IL-6 and TGF-alpha
- These results confirm the indication of initial corticosteroid therapy in bacterial meningitis

## 2. Encephalitis and other neuro-invasive infections as a sentinel of emerging infections

## Regional Impact of Climate on Japanese Encephalitis in Areas Located near the Three Gorges Dam

Y. Bai et al. PLoS ONE 2014; 9(1): e84326. doi:10.1371/journal.pone.0084326

- Objective : To identify key climatic factors associated with the transmission of JEV in areas located near the Three Gorges Dam (China), between 1997 and 2008.
- Results (statistically significant): JEV incidence was negatively related to rainfall and positively to temperature raise.
- Conclusion : the surveillance of neurological presentation of a vector-borne infection is effective for the detection of changes in trends and emergence

**West Nile virus: review of the literature.**  
LR Petersen et al. JAMA. 2013, 310:308-15

- West Nile Virus is now endemic in the USA, with 16,196 human neuroinvasive disease cases and 1,549 deaths reported since 1999
- Neuro-invasive infections occur in less than 1%
- This presentation is the easiest way to monitor the outbreaks, epidemiological trends and evolution of the viral strains

# The year in tuberculosis, a high burden in resource-limited countries



## Contact investigation for active tuberculosis among child contacts in Uganda

D. Jaganath et al. C.I.D. 2013; 57:1685-92

- 761 contact children (< 15 year old), from 351 households
- Prevalence of TB in this population: 10%, of which 71% were culture-confirmed
- HIV-positive rate was 3%

## Contact investigation for active tuberculosis among child contacts in Uganda

D. Jaganath et al. C.I.D. 2013; 57:1685-92

- Risk factors for active tuberculosis in child contacts (multivariable logistic regression)
  - Younger age (< 5 y.o.)
  - HIV infection
  - Positive tuberculin skin test
  - Independent of sex, BCG scar, nutritional status
  - In older children (> 5 y.o.), sleeping in the same bed was the only significant risk factor



## Contact investigation for active tuberculosis among child contacts in Uganda

D. Jaganath et al. C.I.D. 2013; 57:1685-92

- Contact investigation is possible
- It detects a lot of TB cases
- It is mandatory in order to reduce TB transmission

And what about MDR  
tuberculosis?

**Preventive therapy for child contacts of multi-drug resistant tuberculosis: a prospective cohort study**

J.A. Seddon et al. C.ID. 2013; 57:1676-84

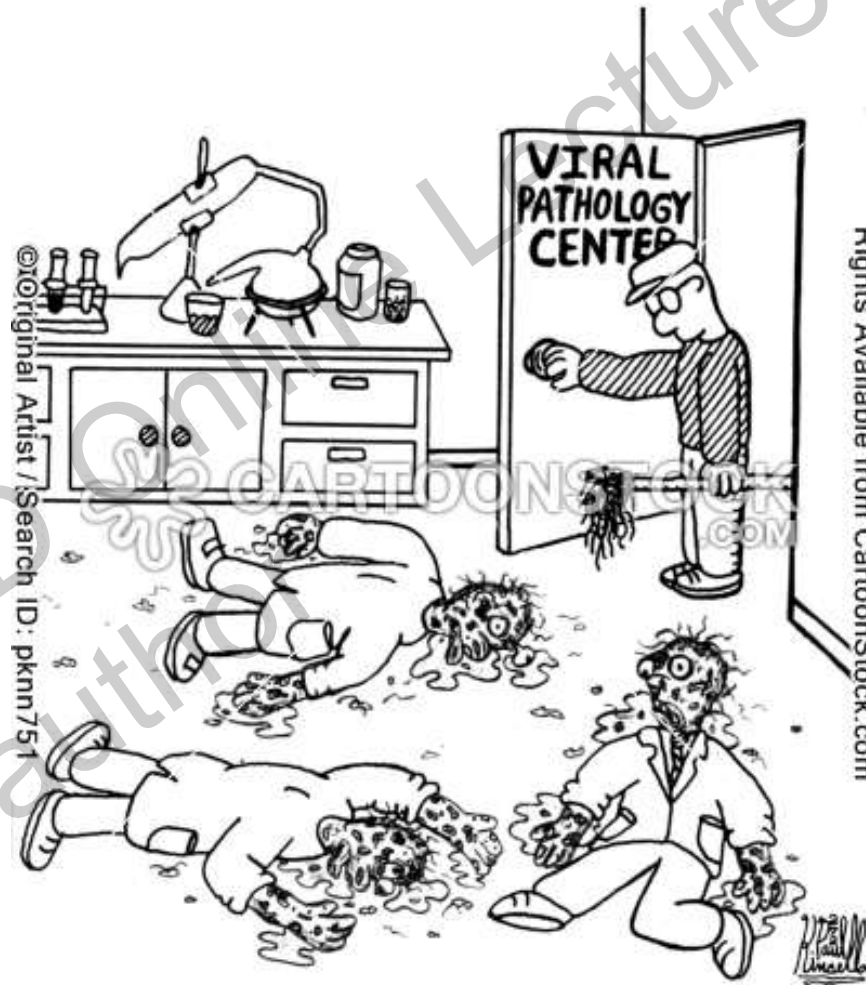
- Prospective cohort, South Africa
- Exposure to ofloxacin-susceptible, MDR tuberculosis index-case
- HIV positive: 5%
- Preventive therapy: ofloxacin (20 mg/kg daily), ethambutol (25 mg/kg daily), high-dose isoniazide (20 mg/kg daily) for 6 months
- Evaluation 2, 4, 6 and 12 months

## Preventive therapy for child contacts of multi-drug resistant tuberculosis: a prospective cohort study

J.A. Seddon et al. C.ID. 2013; 57:1676-84

- Results :
  - 186 children included, as contacts of 164 index patients
  - No adverse events required the discontinuation of the treatment
  - 1 onset of tuberculosis in a HIV-negative child despite good observance of the treatment

# Emerging or re-emerging infections



**Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study**

Assiri A et al, Lancet Infect Dis. 2013; 13(9):752-61.

- 46 adults and 1 child, sex ratio M/F =3.3
- 28 patients died → 60% case-fatality rate (rising with the older age)
- 96% of patients had underlying comorbid medical disorders
  - diabetes (68%),
  - hypertension (34%),
  - chronic cardiac disease (28%),
  - chronic renal disease (49%).
- chest radiography: from subtle to extensive unilateral and bilateral abnormalities in 100% patients

# Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease from Saudi Arabia: a descriptive study

Assiri A et al, Lancet Infect Dis. 2013; 13(9):752-61.

## ➤ Symptoms:

- fever (98%), fever with chills or rigors (87%),
- cough (83%),
- shortness of breath (72%),
- myalgia (32%).
- diarrhoea (26%), vomiting (21%), abdominal pain (17%).

## ➤ Blood biochemistry and cells

- increased dehydrogenase (49%)
- Increased aspartate aminotransferase (15%)
- thrombocytopenia (36%)
- lymphopenia (34%).



# MERS-Cov vectors



- **Middle East respiratory syndrome coronavirus in bats, Saudi Arabia**

Memish ZA, et al. Emerg Infect Dis. 2013 Nov;19(11):1819-23.

- **Middle East respiratory syndrome coronavirus infection in dromedary camels in Saudi Arabia**

Alagaili AN, et al. MBio. 2014 Mar 25;5(2). pii: e01002-14. doi: 10.1128/mBio.01002-14



# MERS-Cov and nosocomial transmission

- **Hospital Outbreak of Middle East Respiratory Syndrome Coronavirus**

Abdullah Assiri et al. N. Eng. J. Med. 2013; 369: 407-16

- **Clinical features and viral diagnosis of two cases of infection with Middle East Respiratory Syndrome coronavirus: a report of nosocomial transmission.**

B. Guery et al. Lancet. 2013; 381(9885):2265-72

# Hepatitis C: a new era?



*"BY THE WAY, I HAVE HEPATITIS C"*

## **Chronic hepatitis C: future treatment**

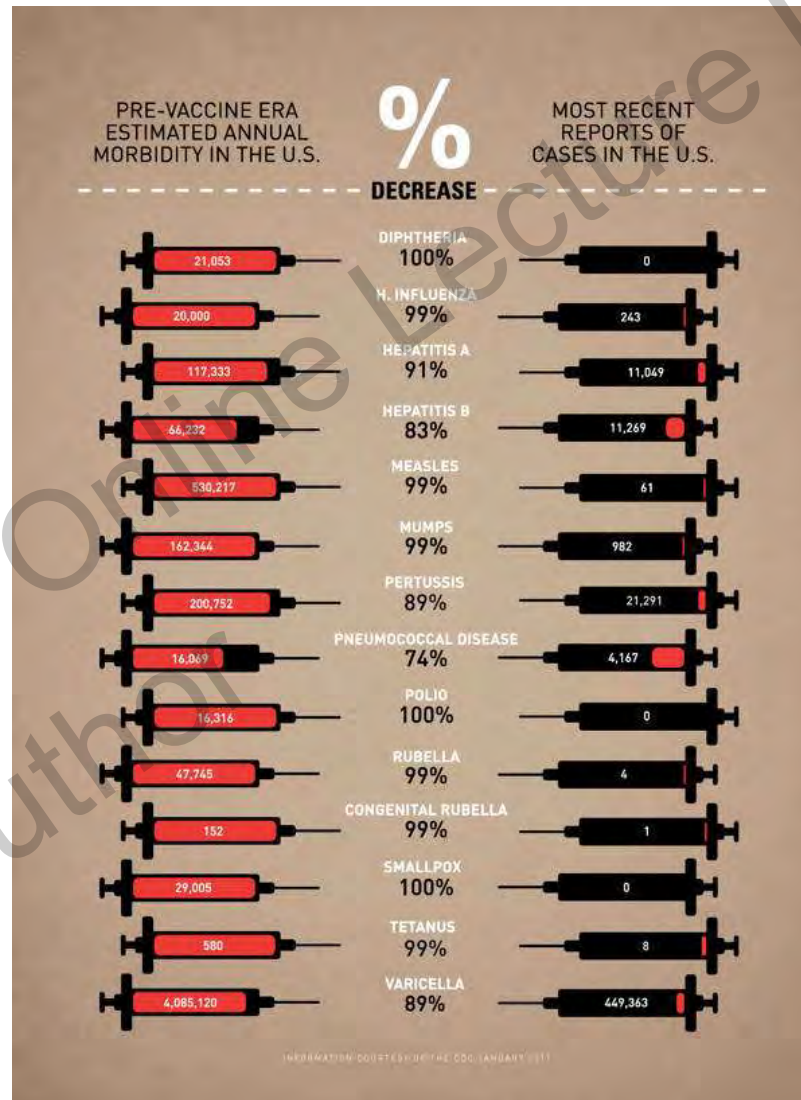
A. Wendt et al. Clin. Pharmacol.: Adv. Applic.; 2014; 6: 1-17

- **New antivirals: toward interferon-free regimens.**
- **Regimens containing sofosbuvir (the most recently marketed product) have a pan-genotypic activity: from 88% to 100% for naïve GT-1, 3, 4 and 6.**

# The future of HCV

- Due to better activity and tolerance, new regimens open the debate:
  - ✓ Should we treat all infected patients, even if don't present with liver fibrosis?
    - It could lead to eradication of the virus,
    - But aren't hygiene measures, currently implemented, efficient enough for the reduction of transmission?
    - Would these patients be spontaneously cured or stabilized, and so treatment could be useless?
    - Anyway the immediate cost would be high.
  - ✓ Should we restrict the use of these drugs to patients presenting with liver fibrosis?

# New available vaccines of the year



**Early Impact of 13-Valent Pneumococcal Conjugate Vaccine on Community-Acquired Pneumonia in Children.** F. Angoulvant et al. Clin Infect Dis. ciu006 first published online February 13, 2014.

- Conjugated anti-Pneumococcal vaccine, including 13 valences. It is efficient in children.
- The impact in adults is still under investigation, but early reports of the study CAPITA demonstrate a decrease in pneumonia in vaccinated adults and elderly.

**Predicted strain coverage of a meningococcal multicomponent vaccine (4CMenB)  
in Europe: a qualitative and quantitative assessment**

U. Vogel et al.

Lancet I.D. 2013; 13: 416-25

- Meningococcus B vaccine, a new protein-based vaccine (4 major proteins), is now approved in Europe, and already recommended in some countries.
- Using MATS (meningococcal antigen typing system), **78%** are estimated to be covered by this vaccine, **50%** of strains being covered by more than one antigen
- The remaining concern is the duration of the immunity.

# Usefull guidelines !

Clinical Infectious Diseases Advance Access published December 4, 2013

IDSA GUIDELINES

## 2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host

An international panel of experts prepared an evidenced-based guideline for vaccination of immunocompromised adults and children. These guidelines are intended for use by primary care and subspecialty providers who care for immunocompromised patients. Evidence was often limited. Areas that warrant future investigation are highlighted.

**Keywords.** vaccination; immunization; immunocompromised patients; immunosuppression; asplenic patients; immunodeficiency patients

<http://cid.oxfordjournals.org/content/early/2013/11/26/cid.cit684.full.pdf+html>



# Antibiotic stewardship



**Impact of rapid organism identification via Matrix-Assisted Laser Desorption/Ionization Time-of-flight combined with antimicrobial stewardship team intervention in adult patients with bacteremia and candidemia.**

Huang A. et al. Clin. Infect. Dis. 2013; 57:1237-45

- The study : Early bacterial identification (MALDI-TOF) and antimicrobial stewardship team intervention, vs conventional culture, identification and antibiogram (preintervention study period)
- 501 patients presenting with bacteremia or candidemia
- Results : decreased time and better outcome in MALDI-TOF group
  - To bacterial identification: 84 to 56 hours
  - To effective antibiotherapy: 30 to 20 hours
  - To optimal antibiotherapy: 90 to 47 hours
  - **Lethality : 20 to 14.5%**

**Infectious Diseases specialty intervention is associated with decreased mortality and lower healthcare costs**

S. Schmitt et al. C.I.D. 2014; 58: 22-31

- Charts review, from 2008 to 2009,
- 101 991 stays with I.D. intervention, vs 170 336 stays without I.D. intervention
- Lower lethality with I.D. intervention: OR = .87 (.83 - .91)
- Patients receiving I.D. intervention within 2 days of admission = lower 30-day lethality (OR = .86; .82-.90)

# Antibiotic stewardship and the general population

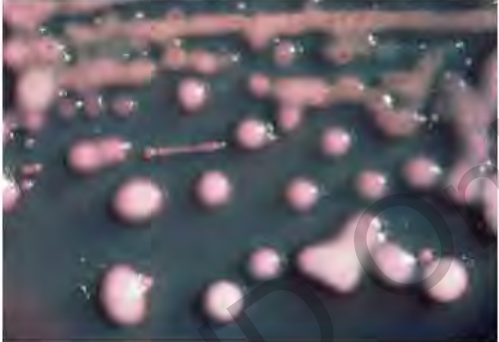
- A major issue is to convince both the general population and politicians about the reality of this future disaster: a world with less and less active antibiotics due to
  - ✓ the lack of research,
  - ✓ the lack of new drugs,
  - ✓ the increasing rate of bacterial resistance
- The following cover page of the New York Times, a worldwide-coverage non-medical journal, and the complete debate dedicated to this topic, is encouraging.

The screenshot shows a web browser window displaying a New York Times article. The browser's address bar shows the URL: www.nytimes.com/roomfordebate/2013/12/29/avoiding-a-time-when-bacteria-can-no-longer-be-stopped. The page header includes the New York Times logo, a search bar, and a 'LOG IN' button. The article is dated December 29, 2013, and is titled 'When Bacteria Can No Longer Be Stopped'. Below the title, there is an 'INTRODUCTION' section with a photograph of pink, rod-shaped bacteria. The text in the introduction states: 'This lethal type of bacteria has become resistant to nearly all antibiotics. Centers for Disease Control and Prevention, via Associated Press. The greatest medical miracle of the 20th century may become useless in the 21st century. Bacterial resistance to antibiotics, seen almost as soon as the medications were developed, has become a serious problem.' To the right of the introduction is a 'DEBATERS' section with six entries, each featuring a small portrait and a headline. The entry 'Uses for Meat Production Are a Minor Problem' by Liz Wagstrom is circled in red. The other debaters and their topics are: David Gilbert (Fight Fear With Science), Brad Spellberg (Government Needs to Aid Industry Research), Louise Slaughter (Mandatory Limits on Farm Use Are Needed), Matti Jalasvuori (Develop Viruses to Fight Resistant Bacteria), and John Bartlett (Adopt a National Plan, Like Europe's Program).

DECEMBER 29, 2013

# When Bacteria Can No Longer Be Stopped

**INTRODUCTION**



This lethal type of bacteria has become resistant to nearly all antibiotics. Centers for Disease Control and Prevention, via Associated Press

The greatest medical miracle of the 20th century may become useless in the 21st century. Bacterial resistance to antibiotics, seen almost as soon as the medications were developed, has become a serious problem.

**DEBATERS**

- Fight Fear With Science**  
DAVID GILBERT, PROVIDENCE PORTLAND MEDICAL CENTER
- Government Needs to Aid Industry Research**  
BRAD SPELLBERG, LOS ANGELES BIOMEDICAL RESEARCH INSTITUTE
- Mandatory Limits on Farm Use Are Needed**  
LOUISE SLAUGHTER, MEMBER OF CONGRESS
- Uses for Meat Production Are a Minor Problem**  
LIZ WAGSTROM, NATIONAL PORK PRODUCERS COUNCIL
- Develop Viruses to Fight Resistant Bacteria**  
MATTI JALASVUORI, RESEARCHER
- Adopt a National Plan, Like Europe's Program**  
JOHN BARTLETT, JOHNS HOPKINS MEDICAL SCHOOL

Although controversial points of view were presented.....

Thank you for your attention

