

What Every HIV Clinician Needs to Know about Infectious Diseases

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Conflicts of Interest: None

THE MENU

- **MACRA: US data**
- **Resistance:
Bad bugs, no drugs**
- **Molecular microbiology**
- **Readiness:
ZIKA etc. & bioterrorism**
- **Microbiome**

MACRA

- **Why:** The US healthcare costs are >2x those of any other country and rank 23d in healthcare outcomes (longevity, infant death, addiction, etc)
- **Plan:** Reimbursement based on volume changed to reimburse based on value (“Value vs Volume”)
- **Clout:** CMS- major US healthcare payer & Joint Commission requirement for stewardship
- **Data:** CDC Source: EHR
- **Evaluation:** needed
- **Concern:** EHR/time demands

CDC: ANTIMICROBIAL USE & RESISTANCE (AUR) Module

Goal: Establish risk-adjusted benchmarks for antimicrobial use by antimicrobial agent, route of treatment (PO, IV, IM) & days of therapy (DOT) analyzed by patient units (medical, surgery, ICUs, pediatrics, obstetrics, outpatients, etc):

JHH: Use of levofloxacin during August 2016

Mo/Yr.	Drug	Total	IV	IM	GI	Resp
8/2016	Cipro	307 Days	234 Days	0	178 Days	0

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Antibiotic Resistance

***Neisseria gonorrhoeae* - azithromycin**

***H. pylori* - macrolides; metronidazole; rifampin**

***S. pneumoniae* - macrolides, amoxicillin**

***Mycoplasma pneumoniae* - macrolides**

***M. tuberculosis* - INH, rifampin, PZA, quinolones**

Influenza - oseltamivir

***Bacteroides fragilis* - clindamycin, moxifloxacin
metronidazole, carbapenems**

***Vibrio cholera* - MDR**

Enterococcus - vancomycin

Major Resistant Pathogens, 4,000 US Hospitals, CDC, March 2016

Major Resistant Bacteria

Recent Data

ESBL <i>Enterobacteriaceae</i>	18%
Enterococcus- VRE	27%
MDR <i>P. aeruginosa</i>	13%
MDR <i>Acinetobacter</i> sp	45%
Carbapenemase + GNB	3%

* 8 states in US, esp. SC and Illinois

WHO Priority Pathogen List

Critical: *A. baumannii* —carbapenem-resistant

P. aeruginosa—carbapenem-resistant

Enterobacteriaceae—carbapenem-resistant

& 3d gen. cephalosporin-resistant

HIGH: Vanco-resistant enterococcus

MRSA—Vanco-resistant

H. pylori—clarithromycin-resistant

Salmonella—FQ-resistant

N. gonorrhoeae—FQ & 3d-gen ceph resist

Antibiotic Resistance Intervention Bundle

- **Short course**
- **Procalcitonin** to guide when to start and stop
- **Peer comparisons +/- report cards**
- **Molecular diagnostics** use and interpretation
- **Automatic stop orders**
- **“Time-out” at 72 hrs:** Review abx, cult, response
- **IV → PO** switch early
- **Gene sequencing** to trace transmission paths
- **Guidelines** from authoritative sources
- **Preauthorization** required

Meeker D. JAMA 2016;316:562

Assessment: Abx prescribing based on audits of 249 primary care MDs for 214,753 RTI visit

Results: Change in prescribing antibiotics at baseline to intervention 24.1% → 13.1%

Most successful: **Accountable justification**

(-17%) & peer comparison (-18%) P <0.001

Postscript: NY Times 3/28/16: Note in EHR to all providers for top 10% and lowest 10%

Recent Antibiotic Recommendations

Acute bronchitis*: No abx & no microbiology

Pharyngitis*: Pos strep test only: beta lactam

Common cold*: “No, never”

Sinusitis**: “Watchful waiting” x >7 days

Asymptomatic UTI*** : No abx due to harm-symptomatic UTI & resistance

*ACP 2016; **Am Acad Otolaryngol. 2015; ***IDSA, 2015

Ciprofloxacin

“Just say no”

FDA-approved 1987-

- * Wide range of indications: UTI, CAP, sinusitis, EACB, cellulitis, IAS, anthrax**
- * WHO—Essential drug**
- * Largest-selling antibiotic in world- \$0.04/pill**

FDA- New warning (July 26, 2016)

- * ADRV—tendonitis, neuropathy, CNS (CDI!!!)**

FDA: “Always use alternatives if possible”

Antibacterial Decision Making: Role of Procalcitonin (?CRP-POC)

Biology: Marker of bacterial replication

Utility: Facilitates decision to start or stop antibacterial agents

Europe: Extensive use POC CRP;
US – minimal

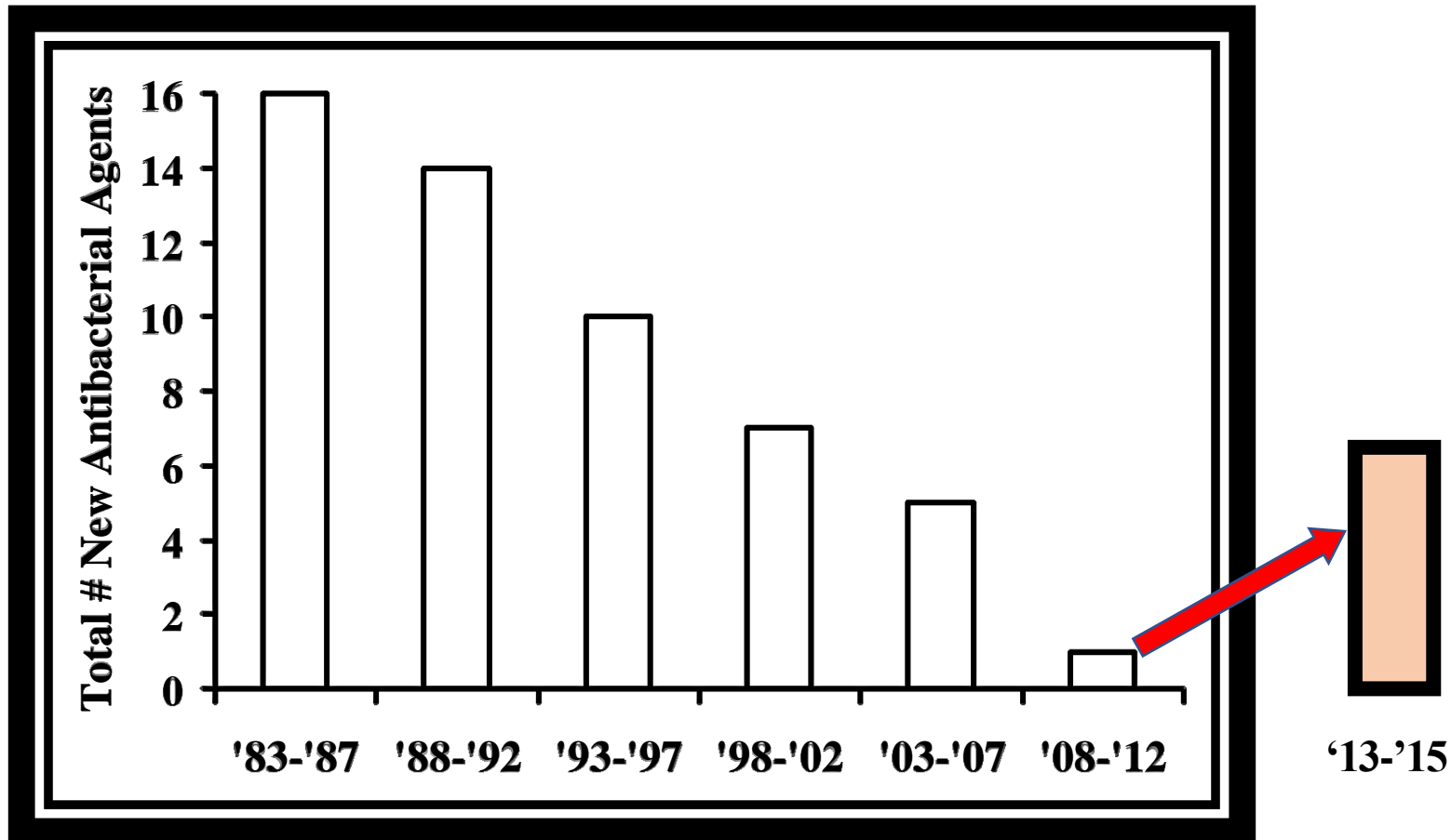
Cochrane review: 7 controlled trials,
1,458 patients: 51% decrease in Abx

(Tang H. Infection 2009;37:497)

Multiple studies show rapid initiation of effective antibiotics for seriously ill patients consistently correlates with improved outcome, including survival

1. **CAP: Survival data mandate starting antibiotics within 4-6 hours (Bratzler; UK)**
2. **New sepsis guidelines recommend initiation of antibiotics within 1 hr. or penalties**

Number of New Antibiotics by Year



IDSA 10 by 20: Scorecard

New abx	FDA Date	Indication	ESCAPE Target
Fidaxomicin	2003	CDI	No
Bedaquiline	2012	TB	No (MDR-TB)
Dalbavancin	2014	ABSSI	No
Tedizolid	2014	ABSSI	No
Oritovancin	2014	ABSSI	No
Ceftaroline	2010	CAP; ABSSI	Yes
Ceft/tazobactam	2014	CAI	Yes
Ceftaz/avibactam	2015	CAI;CUTI	Yes

ABSSI-acute skin/STI; IAI-intra-abd Inf; CUTI-complex UTI

Ceftolozane/Tazobactam (CID 2016;63:234)

Class: 2nd-gen cephalosporin/beta lactamase inhibitor

Spectrum: Active vs most enteric GNB

Special advantage: Active vs **ESBL and some multiply resistant *P. aeruginosa***


Dose: 1.5 gm q 8 hrs infused over 1 hr; renal dosing

T1/2: Ceftolozone- 3 hr/tazobactam-1 hr

Cost: \$240/day; doripenem-\$120; imipenem- \$50;
Cefepime- \$16; pip/tazo-\$40; cefotaxime- \$10

FDA Approval: Complicated UTIs & intra-abdom infect

Ceftazidime-Avibactam: Activity (Sader H. AAC 2014;58:1692)

In vitro activity clinical isolates: % sensitive				
Microbe	N	Ceft	Ceft/Avi	Mero
All coliforms	640	89%	100%	99%
Klebsiella	1,847	100%	99%	94%
E. coli	767	92%	100%	99%
Morganella	295	86%	100%	100%
P. aeruginosa	1,967	83%	97%	82%
 ESBL +	328	31%	97%	99%

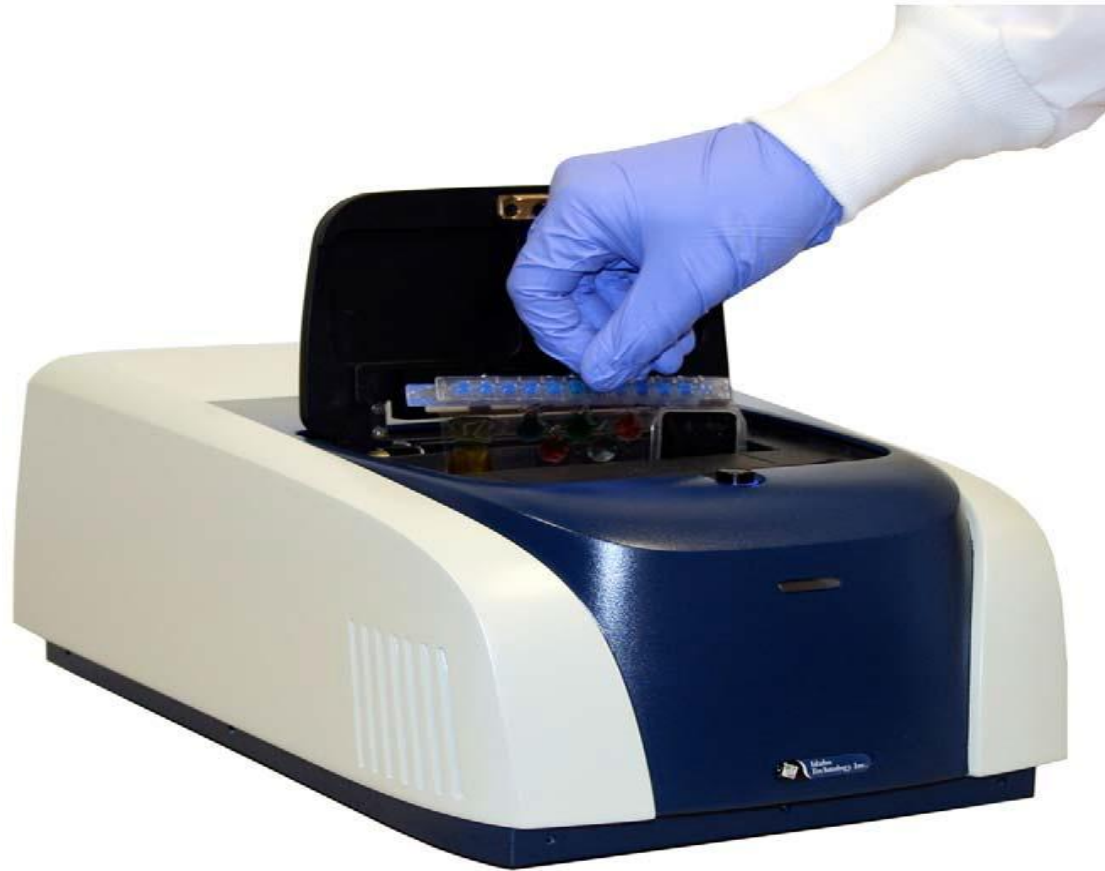
New Antibiotics in Development

- * IV minocycline: *Acinetobacter* sp,
Stenotrophomonas, *Burkholderia* sp
- * New polymyxins: non-nephrotoxic
- * Meropenem/RPX7009: carbapenemase
inhibitors - KPC, *A. baumannii*, *P. aeruginosa*
- * Plazomicin

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FilmArray



FDA-cleared Nucleic Acid Amplification Tests (NAAT)

- **Viruses**: Measles, mumps, varicella, RTI-rhinovirus, coronavirus, enterovirus, adenovirus, HMPV, RSV, parainfluenza, influenza, encephalitis- WNV, HSV, JCV; Other- EBV, dengue, HPV, BK virus, rabies, CMV

- **Bacteria**: GC, *C. trachomatis*, *M. pneumoniae*, Legionella, *C. dif.*, *T. whipplei*, *B. bergdorferi*, *M. tuberc.*, Coxiella, Ehrlichia, Strep A,B,C,G

- **Other**: Trichomonas, PCP

BioFIRE FILM ARRAY- GI Panel

(Buss SN. J Clin Micro 2015;53:379)

Method: 4 sites; 1,555 specimens; BioFIRE vs lab standard

Result: Pathogen BioFire Control Sensitivity

<i>C. jejuni</i>	58	35	97%
<i>C. difficile</i>	204	165	99%
Salmonella	37	31	100%
Shigella	47	49	96%
ETEC	38	22	99%
EPEC	348	317	99%
Cryptosporidium	18	24	100%
Norovirus	70	55	95%

Plex-ID: The Next-Generation System: T5000

IBIS T5000



RT- PCR → Electron
ionization – mass spec
Detects bacteria, viruses,
and fungi

Result: <8 hr (expect 3 hrs)

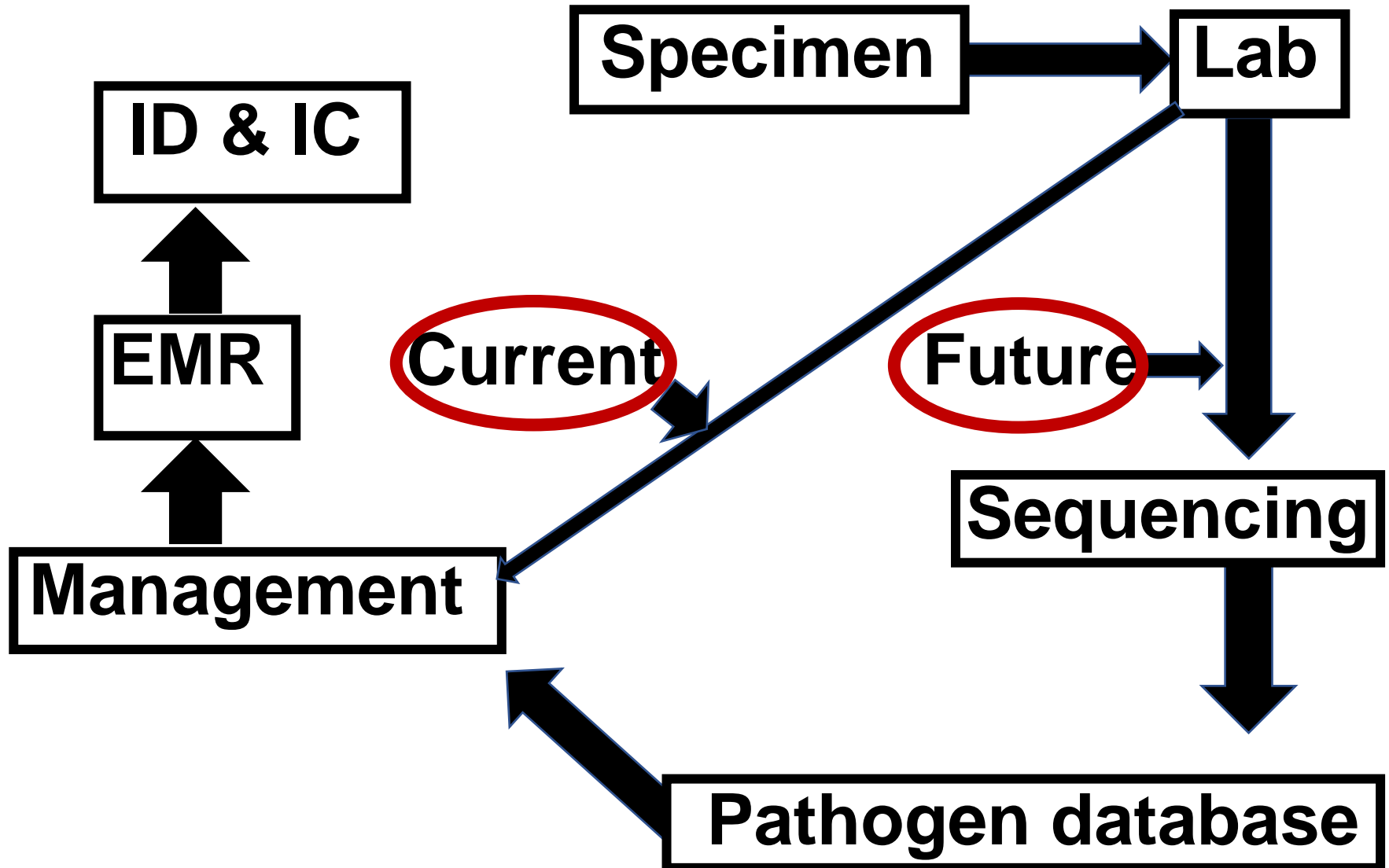
Quantitative

Cost: \$500K,

\$80/sample

Next-generation Sequencing

Pak TR & Kasarskis A. CID 2015;61:1695



CDI: British Health System

NHS: CDI epidemic throughout the UK

Decrease rate mandate Fired Administrators

Response:

- 1) Epidemiology: NAP-1
- 2) "Stopped" FQ (+ cephalosporins)
- 3) Gene sequencing- infection control

Result: Rates ↓ 80%!

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The Next Epidemic- Lessons from Ebola (Bill Gates. NEJM 2015;372:1381)

Issue: **Medical leaders never seem ready**

Examples: Flu-1918; HIV; SARS

Precedent: War – NATO

Last example of preparing for pandemic: Dark Winter- Smallpox (Inglesby T. CID; 2002;34:972)

Recommended components: 1) Health systems; 2) surveillance; 3) trained respondents; 4) good data; 5) diagnostics, vaccines, drugs

Microbial Epidemics That Usually Required Local Engagement

Toxic shock-*S. aureus*

AIDS

West Nile virus

Lyme disease

H1N1; H5N1 influenza

SARS

MERS

S aureus USA-300

Legionella

Hepatitis C

C difficile NAP-1 strain

Measles, mumps

Anthrax (bioterrorism)

Iatrogenic fungal meningitis

Foodborne: salmonella,

Listeria, *E. coli* 0157

Ebola

Zika virus



Persistence

& STDs

Mosquito-borne Travelers' Infections

* **Dengue**: (“Bone-break”)

* S. America 1990s

* **West Nile virus**: US-1999

* **Chikungunya**: “Bent-up”

Reunion Island at 1 yr
- 44% still had disabling arthritis
(Medicine. 2012;91:212)

* **Zika virus**: Uganda; fever, rash, joint pain 2015

S. America (esp. Brazil), Caribbean; 40 M/yr; then Florida
New- Neurotrophic; pregnancy complication; STD; persistence

* **Yellow fever**: Now epidemic in Brazil; clinically the most serious with 3.5%-7.5% mortality.

Common to all- ***A. aegypti*** mosquito vector

Fauci A. NEJM. 2016;374;601.



Bioterrorism

2001: The event using *B anthracis* (anthrax)

Anthrax: spore form; inert & stable for decades in all conditions;
vegetative form: highly lethal

Distribution: Mail to politicians and journalists

Final data: 15 cases with 5 deaths and massive panic

Major bioterrorism agents: Anthrax and smallpox

Who: Russia, Iraq, & N. Korea

Data source for Russia: K. Alibek: Responsible for Russian bioterrorism program, then defected to US and authored book on Soviet program- >20 metric tons of weaponized smallpox.

Planning: CDC: Smallpox-

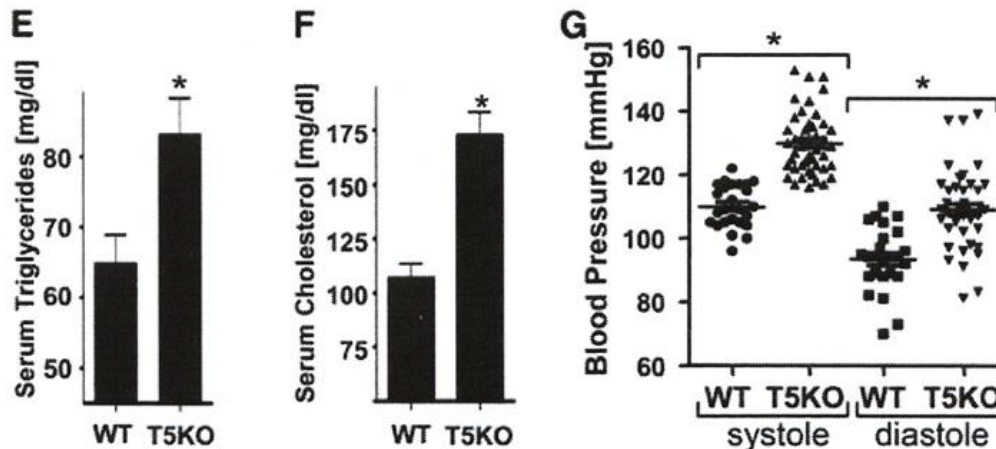
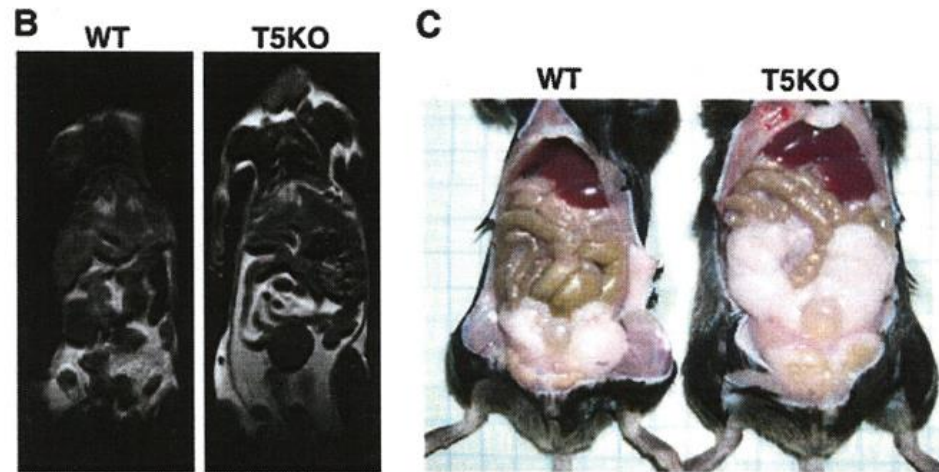
New guideline, antibiotic and vaccine

(for the only pathogen “eliminated” from globe)

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Metabolic Syndrome with Fecal Transplant in Rodent Model



Openbiome- Commercial Stool for Transplant for Relapsing CDI: (openbiome.com)

Donors: 2.5 hr interview for acceptability- diet, activities, health, GI disease, wt, BMI, abx, etc., CRE, ESBL, MRSA: 2.8% accepted

Donors: Stool donated 3X/week

Product: Available for \$385, shipped to 50 states and 7 countries frozen on dry ice (nonprofit)

No. shipped: 17,572;

Outcome – Successful: 87%

Wt gain: <2%; **Plan:** Eradicate mcr-1 gene?

Plan: NIH-funded: 5-year changes—wt, DM, lipids

ID Review 2017: Summary

Abx resistance is a crisis that was predicted in 2006

Response is **antibiotic stewardship**— major role in clinical care is “smart use” of antibiotic.

The **CDC/CMS MACRA plan**: Expect audits of use by EHR for comparison with benchmarks & ?EHR review by health facility, service, DRG, provider.

Molecular micro will transform the micro lab; need caution

C. dif- High **CMS/CDC priority** to reduce (like UK); stool transplant is “hot” & may have a transformative future

ID always has surprises: 2015-Ebola; 2016- Zika; 2017-?



The END

HIV Management
Hepatitis Management

THE NEW YORK COURSE

