



Hospital Updates in Infectious Diseases Puerto Rico ACP 2020

Daniel C. DeSimone, MD
Consultant, Infectious Diseases
Mayo Clinic

Disclosures for speaker:

Date of presentation: 3/13/2020

- No relevant financial disclosures:
 - Daniel C. DeSimone, MD
- *Reference to off-label/investigational use(s) of pharmaceuticals or devices:*
 - None

Outline

- 1st line therapy for C. difficile infection
- De-escalation of MRSA coverage in HAP
- PO therapy for left sided endocarditis
- COVID-19

Background

- For 30 years, metronidazole and oral vancomycin have been the main antibiotic agents used in the treatment of CDI
- More recent randomized RCTs have shown that oral vancomycin was superior to metronidazole

Metronidazole is no longer 1st line therapy

- In settings where access to vancomycin or fidaxomicin is limited, we suggest using metronidazole for an **initial episode of nonsevere CDI only**
- The suggested dosage is metronidazole 500 mg orally 3 times per day for 10 days.
- Avoid repeated or prolonged courses due to risk of cumulative and potentially irreversible neurotoxicity

CDI Treatment

- Discontinuation of antibiotics and acid-suppression medications (eg, proton pump inhibitors, H2 blockers) if possible, and avoidance of antiperistaltic agents that may obscure symptoms and precipitate complicated disease

C. Difficile infection

Antimicrobial agents that may induce *Clostridioides* (formerly *Clostridium*) *difficile* diarrhea and colitis

Frequently associated	Occasionally associated	Rarely associated
Fluoroquinolones	Macrolides	Aminoglycosides
Clindamycin	Trimethoprim-sulfamethoxazole	Tetracyclines
Cephalosporins (broad spectrum)		Metronidazole
Penicillins (broad spectrum)		Vancomycin

Assessing disease severity

- **Non-severe**
 - Absence of any severe or fulminant criteria
- **Severe** (any 1 of the following criteria)
 - WBC > 15,000 cells/mm³; Creatinine > 1.5 mg/dL; Albumin < 3 g/dL
- **Fulminant**
 - Admission to ICU
 - Hypotension or Shock
 - Ileus or significant abdominal distention
 - WBC ≥ 35,000 cells/mm³ or < 2,000 cells/mm³
 - Serum lactate level > 2.2 mmol/L
 - End-organ failure
 - Megacolon

Clinical Definition	Supportive Clinical Data	Recommended Treatment ^a
Initial episode, non-severe	Leukocytosis with a white blood cell count of $\leq 15,000$ cells/mL and a serum creatinine level < 1.5 mg/dL	<ul style="list-style-type: none"> • VAN 125 mg given 4 times daily for 10 days, OR • FDX 200 mg given twice daily for 10 days • Alternate if above agents are unavailable: metronidazole, 500 mg 3 times per day by mouth for 10 days
Initial episode, severe ^b	Leukocytosis with a white blood cell count of $\geq 15,000$ cells/mL or a serum creatinine level > 1.5 mg/dL	<ul style="list-style-type: none"> • VAN, 125 mg 4 times per day by mouth for 10 days, OR • FDX 200 mg given twice daily for 10 days
Initial episode, fulminant	Hypotension or shock, ileus, megacolon	<ul style="list-style-type: none"> • VAN, 500 mg 4 times per day by mouth or by nasogastric tube. If ileus, consider adding rectal instillation of VAN. Intravenously administered metronidazole (500 mg every 8 hours) should be administered together with oral or rectal VAN, particularly if ileus is present.

VAN—Vancomycin
FDX--Fidaxomicin

Number of episodes

- **Recurrent CDI**

- Symptom recurrence (loose or watery stools for 2 days)
- Positive stool test for *C. difficile* **within 8 weeks** of prior infection after symptom resolution
- Recurrent infection >8 weeks **without** new or additional risk factors is considered a delayed recurrence and managed as a recurrent infection

- **Re-infection**

- If symptoms resolve and then a future episode develops following exposure to new or additional risk factors, consider the condition as a re-infection and treat as if it were a de novo infection

First recurrence	...	<ul style="list-style-type: none"> • VAN 125 mg given 4 times daily for 10 days if metronidazole was used for the initial episode, OR • Use a prolonged tapered and pulsed VAN regimen if a standard regimen was used for the initial episode (eg, 125 mg 4 times per day for 10–14 days, 2 times per day for a week, once per day for a week, and then every 2 or 3 days for 2–8 weeks), OR • FDX 200 mg given twice daily for 10 days if VAN was used for the initial episode
Second or subsequent recurrence	...	<ul style="list-style-type: none"> • VAN in a tapered and pulsed regimen, OR • VAN, 125 mg 4 times per day by mouth for 10 days followed by rifaximin 400 mg 3 times daily for 20 days, OR • FDX 200 mg given twice daily for 10 days, OR • Fecal microbiota transplantation^c

Fidaxomicin

Side Effects	Hy Vee	\$4,714 est retail price	\$3,992.21 with free coupon	GET FREE COUPON
Images	Schnucks Pharmacy	\$4,714 est retail price	\$4,002.05 with free coupon	GET FREE COUPON
GoodRx Care	Costco	\$4,714 est retail price	\$4,012.40 with free coupon	GET FREE COUPON
	Gerbes Pharmacy	\$4,714 est retail price	\$4,148.88 with free coupon	GET FREE COUPON

PO Vancomycin (Generic) Brand--\$4000

Costco	\$108 est retail price	\$108.17 retail price	LEARN MORE
Hy Vee	\$1,145 est retail price	\$112.15 with free discount	GET FREE DISCOUNT
Schnucks Pharmacy	\$877 est retail price	\$112.65 with free discount	GET FREE DISCOUNT
Kroger Pharmacy	\$1,039 est retail price	\$126.68 with free coupon	GET FREE COUPON

PO Metronidazole

Schnucks Pharmacy	\$5 est retail price	\$4.79 with free coupon	GET FREE COUPON
Walmart	\$16 est retail price	\$7.80 with free discount	GET FREE DISCOUNT
Walmart Neighborhood Market		\$7.80 with free discount	GET FREE DISCOUNT

HAP

- Pneumonia that occurs 48 hrs or more after admission w/o signs/symptoms of pneumonia at the time of admission
- Empiric therapy for HAP—cover MRSA, *Pseudomonas aeruginosa*, and other GNB
- Goal: Early aggressive treatment with early and aggressive de-escalation to minimize risk of adverse drug effects, CDI, ABX resistance

Risk factors for MRSA:

- Treatment in a unit in which >20 percent of *Staphylococcus aureus* isolates are methicillin resistant
- Treatment in a unit in which the prevalence of MRSA is not known
- Colonization with OR prior isolation of MRSA

Guidelines

- Current guidelines do not provide guidance on de-escalation before respiratory culture results are available—which may take up to 4 days to process

MRSA

- *S. aureus* including MRSA is a common colonizer of the nares.
- Absence of MRSA nares colonization has reported to be a negative predictor of MRSA pulmonary infections—specifically pneumonia
- Testing can be performed routinely and results <24 hours



MRSA nares swab

- Recent meta-analysis showed nares screening for MRSA had a high specificity (96.5%) and NPV (98.1%) for ruling out MRSA pneumonia
- Negative MRSA nares swab result should lead to more rapid discontinuation of IV Vancomycin

Use of PO ABX for Left-sided Endocarditis

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

JANUARY 31, 2019

VOL. 380 NO. 5

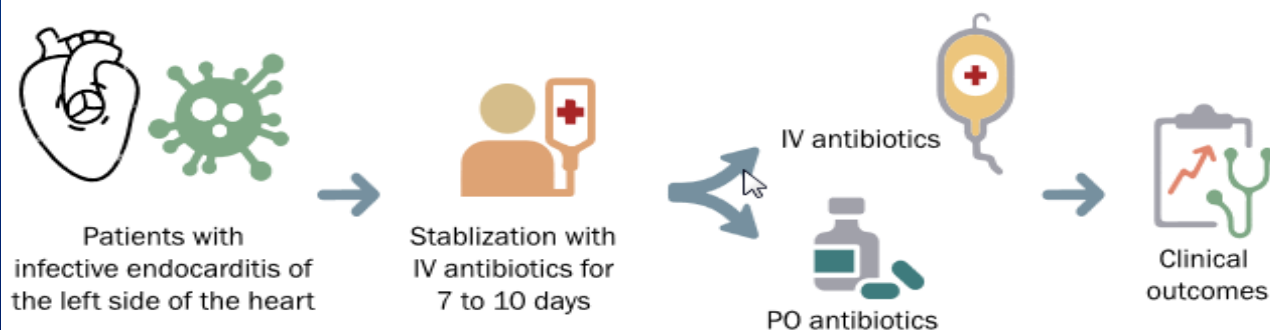
Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis

Kasper Iversen, M.D., D.M.Sc., Nikolaj Ihlemann, M.D., Ph.D., Sabine U. Gill, M.D., Ph.D.,
Trine Madsen, M.D., Ph.D., Hanne Elming, M.D., Ph.D., Kaare T. Jensen, M.D., Ph.D.,
Niels E. Bruun, M.D., D.M.Sc., Dan E. Høfsten, M.D., Ph.D., Kurt Fursted, M.D., D.M.Sc.,
Jens J. Christensen, M.D., D.M.Sc., Martin Schultz, M.D., Christine F. Klein, M.D., Emil L. Fosbøll, M.D., Ph.D.,
Flemming Rosenvinge, M.D., Henrik C. Schönheyder, M.D., D.M.Sc., Lars Køber, M.D., D.M.Sc.,
Christian Torp-Pedersen, M.D., D.M.Sc., Jannik Helweg-Larsen, M.D., D.M.Sc., Niels Tønder, M.D., D.M.Sc.,
Claus Moser, M.D., Ph.D., and Henning Bundgaard, M.D., D.M.Sc.

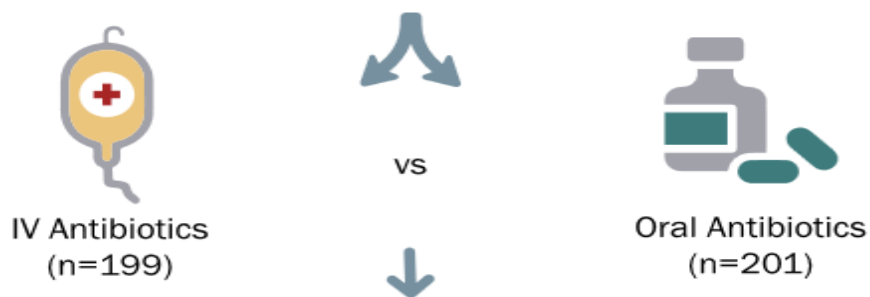
P O E T

Multicenter, randomized, unblinded, noninferiority trial

Objective: To assess the efficacy of shifting to oral antibiotics in endocarditis after stabilization as compared to continuing on IV antibiotics.



400 patients with left sided endocarditis after stabilization were randomized to



Primary Outcome

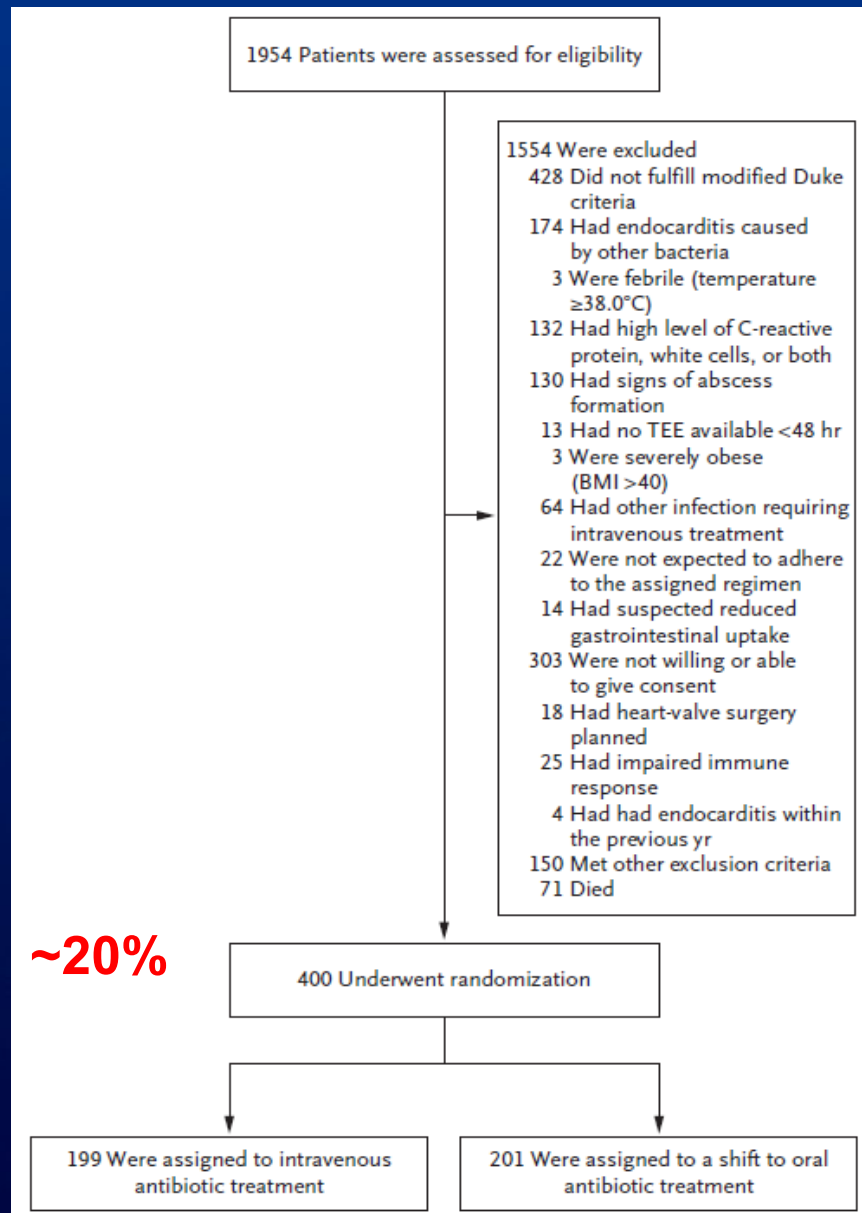
composite of all-cause mortality, cardiac surgery, embolic events, or relapse of bacteremia
between-group difference,
3.1 percent points, 95% CI, -3.4 to 9.6

12.1%

9.0%

P=0.40

In patients with endocarditis on the left side of the heart who were in stable condition, changing to oral antibiotic treatment was noninferior to continued intravenous antibiotic treatment.



POET

- 46% Streptococcus, 25% *E. faecalis*, 23% MSSA, 0% MRSA, 6% CONS
- 79% males, 27% prosthetic valve, 10% PPM,
- 10% multi-valve, 54% AV only, 36% MV only
- F/U in clinic 2-3 times a week until completion; F/U at 1 week, 1, 3, and 6 months

Antibiotic regimens in the POET trial.

	Oral regimens	Frequency n (%)
<i>Staphylococcus aureus</i>	Dicloxacillin and rifampicin	15 (33)
	Amoxicillin and rifampicin	13 (29)
	Moxifloxacin and rifampicin	3 (7)
	Amoxicillin and fusidic acid	2 (4)
	Dicloxacillin and fusidic acid	2 (4)
	Fusidic acid and linezolid	2 (4)
	Rifampicin and linezolid	2 (4)
	Penicillin and rifampicin	1 (2)
	Amoxicillin and clindamycin	1 (2)
	Ampicillin and rifampicin	1 (2)
	Moxifloxacin and fusidic acid	1 (2)
	Moxifloxacin and linezolid	1 (2)
	Linezolid and clindamycin	1 (2)
<i>Enterococcus faecalis</i>	Amoxicillin and moxifloxacin	24 (47)
	Amoxicillin and linezolid	13 (25)
	Amoxicillin and rifampicin	6 (12)
	Moxifloxacin and linezolid	5 (10)
	Amoxicillin and ciprofloxacin	2 (4)
	Amoxicillin	1 (2)

Streptococci	Amoxicillin and rifampicin	47 (52)
	Amoxicillin and moxifloxacin	12 (13)
	Rifampicin and linezolid	8 (9)
	Moxifloxacin and linezolid	8 (9)
	Amoxicillin and linezolid	7 (8)
	Penicillin	3 (3)
	Ampicillin and moxifloxacin	1 (1)
	Ampicillin and rifampicin	1 (1)
	Dicloxacillin and moxifloxacin	1 (1)
	Moxifloxacin and clindamycin	1 (1)
	Moxifloxacin and vancomycin	1 (1)
Coagulase negative staphylococci	Fusidic acid and linezolid	5 (38)
	Rifampicin and linezolid	4 (31)
	Amoxicillin and linezolid	1 (8)
	Dicloxacillin and rifampicin	1(8)
	Moxifloxacin and linezolid	1(8)
	Rifampicin and Fusidic acid	1(8)

Results

Table 2. Distribution of the Four Components of the Primary Composite Outcome.*

Component	Intravenous Treatment (N = 199)	Oral Treatment (N = 201)	Difference	Hazard Ratio (95% CI)
	<i>number (percent)</i>		<i>percentage points (95% CI)</i>	
All-cause mortality	13 (6.5)	7 (3.5)	3.0 (–1.4 to 7.7)	0.53 (0.21 to 1.32)
Unplanned cardiac surgery	6 (3.0)	6 (3.0)	0 (–3.3 to 3.4)	0.99 (0.32 to 3.07)
Embolic event	3 (1.5)	3 (1.5)	0 (–2.4 to 2.4)	0.97 (0.20 to 4.82)
Relapse of the positive blood culture†	5 (2.5)	5 (2.5)	0 (–3.1 to 3.1)	0.97 (0.28 to 3.33)

POET

- **Conclusion:** Stable, left sided IE, changing to PO ABX was non-inferior to continued IV ABX
- No differences in primary outcome by age, sex, diabetic status, kidney disease status, pathogen type, surgical management, prosthetic vs native valve type, or involved valve
- No difference in adverse effects between groups

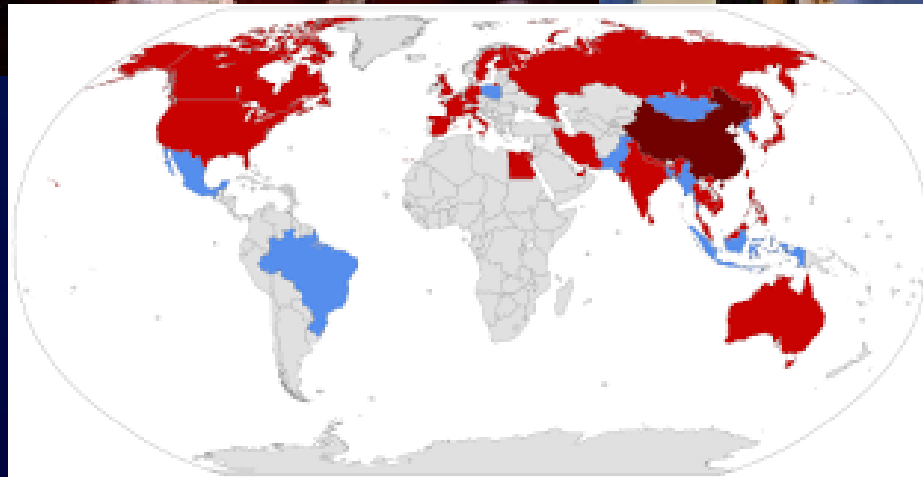
Comments

- Highly selected group of patients, with only 201 patients received PO ABX (from 1954 pts)
 - Affects generalizability of the results
- No MRSA cases
- Few IVDU (5/400)
- ~1/2 had streptococcal IE, 1/4 MSSA
- OPAT program—US vs. Netherlands

Going forward/Practice

- Similar to short course therapy for SAB
 - **It works if you pick'em right**
- PO ABX could be used as a step down for rare, highly selected patients with pathogens susceptible to PO ABX if
 - They are closely monitored
 - Clearly responded and doing well with initial IV treatment

COVID-19



COVID-19

- Novel coronavirus
- Virus name: SARS CoV-2
- Disease it causes: Coronavirus disease 2019 (COVID-19)
- 1/30/2020 WHO declared a PHEIC

SARS CoV-2 (COVID-19)

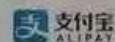
- Betacoronavirus like MERS CoV and SARS CoV
- Origin of all 3 → Bats



大众畜牧野味

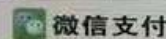


品名	价格	品名	价格	品名	价格	品名	价格	品名	价格	品名	价格	品名	价格
活孔雀	500/只	活鸭豚		活蝎子	500	狐狸肉	45	活豚鼠	40	鹿 脯	38	鳄鱼尾	45
孔雀肉	350/只	活珍珠鸡		活蜗牛	15	活狼仔	75	活荷兰猪	40	鹿 血	100/只	鳄鱼掌	60
活大雁	120	活贵妃鸡		蜗牛肉	30	狼仔肉	20/45	活藏香猪	30	鹿 筋	100	鳄鱼鞭	40/根
大雁肉	15	鹌 鹑	15/只	蜂 蛹	150	活果子狸	130	活豪猪	45	干鹿筋	150	鳄鱼肚	30
去骨大雁肉	15	土 鸽	18/只	蚕 蛹	15	果子狸肉	70	活湘猪	30	鹿 茸	1500	鳄鱼舌	35
活鸿雁		铁 雀		蚂 蚱	100/只	活刺猬	18	香猪肉	25	鹿里脊	50	鳄鱼肠	30
活火鸡	28	活白鹅		木 虫		刺猬肉	8/只	牦牛肉	30	袋装鹿肉	30	活鳄鱼龟	25
活斗鸡	500/只	香椿鸟	15/只	竹 虫	75	活狗狸獾	25	牦牛掌	45	鹿 鞭	400/根	活山鱼	90
活野鸡	60	活鸵鸟	4000/只	活竹鼠	85	活猪狸獾	28	骆驼肉	30	鹿 排	38	活山瑞甲鱼	55
野鸡肉	25/只	鸵鸟肉	45	竹鼠肉	75	花猪肉	25	骆驼掌	45	活鹿子	55	活水貂	500/只
斑 鸠	18/只	鸵鸟掌	80	活麝香鼠		活石头猪	30	骆驼峰	20	鹿子肉	40	活树熊	70
竹 鸡	15/只	鸵鸟肾	45	活青根貂	60	狍子肉	25	活梅花鹿	50	娃娃鱼苗	60/只	带皮乌梢蛇	60
藏 鸡	90/只	鸵鸟蛋	150/个	活海狸鼠	30	杂交野猪肉	15	小活鹿	6000/只	活娃娃鱼	65	去皮乌梢蛇	60
线 鸡		野山羊	40/只	袋鼠肉		野猪肚	120	鹿白条	35	活鳄鱼	40	大蛇条肉	40
育核鸟	15/只	毛野兔	25	松鼠肉		活野猪	25	冷鲜鹿肉	38	鳄鱼肉	40	活海蛇	220
蜈 蚣	5/斤	金 蝉	70	活狐狸	500/只	野猪肉	26	鹿 腿	40	鳄鱼苗	250/只	活虎纹蛙	



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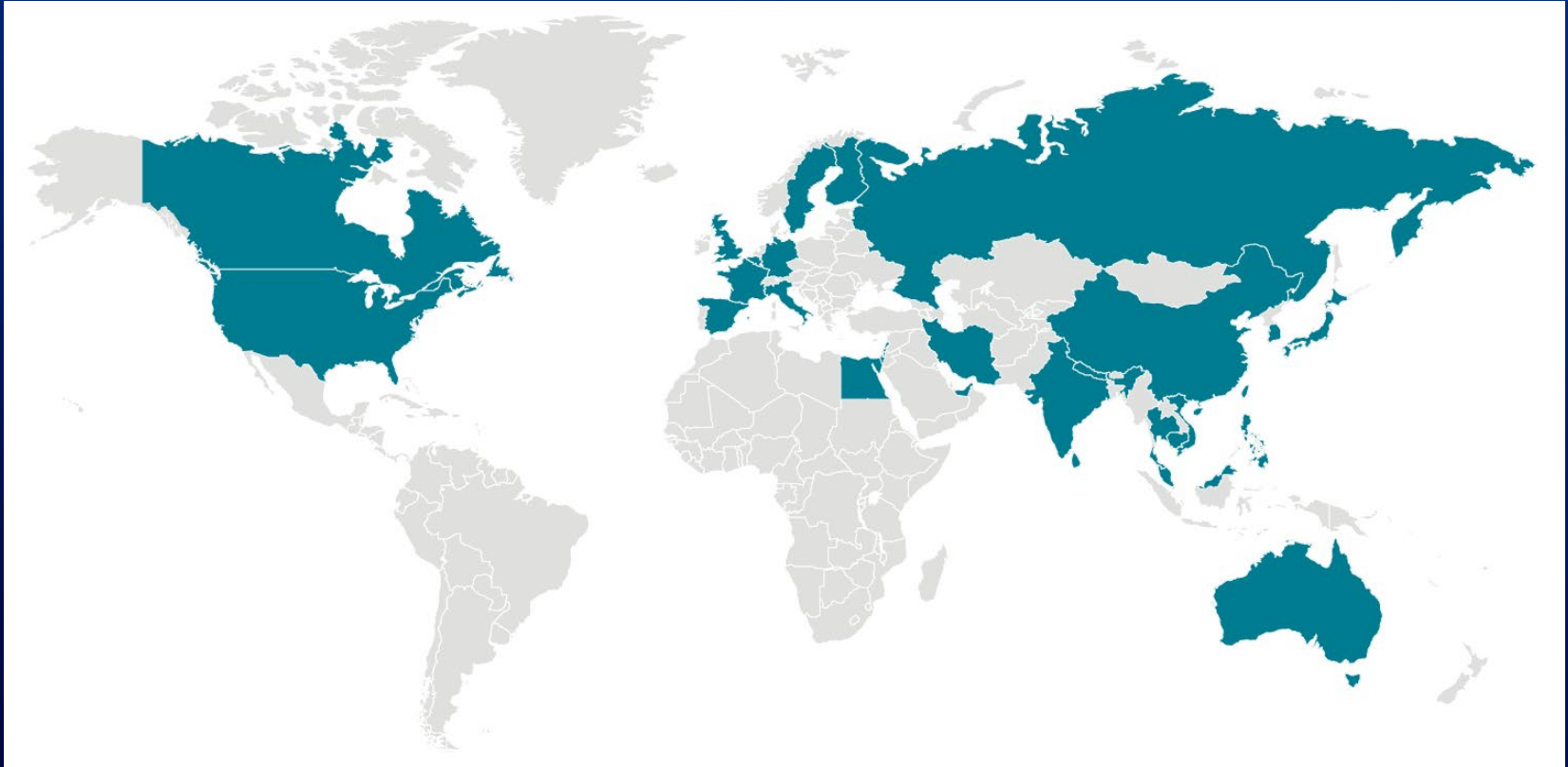
@阎小骏

Testing

- CDC has developed a real time Reverse Transcription-Polymerase Chain Reaction (rRT-PCR) test that can diagnose COVID-19 in respiratory samples from clinical specimens



Locations with confirmed COVID-19 cases as of 2/22/2020



COVID-19

- Spreads from person-to-person
- Symptoms—fever, respiratory illness, within 14 days after travel from China or close contact to someone who has recently traveled from this area (as of 2/23/2020)
- Testing—only conducted at CDC. Health departments who identify a PUI—immediately notify CDC's Emergency Operations Center to report the PU and determine whether testing is indicated. EOC will assist with collecting/storing/shipping specimens.

Coronavirus Disease 2019 (COVID-19) Hospital Preparedness Assessment Tool



All U.S. hospitals should be prepared for the possible arrival of patients with Coronavirus Disease 2019 (COVID-19). All hospitals should ensure their staff are trained, equipped and capable of practices needed to:

- Prevent the spread of respiratory diseases including COVID-19 within the facility
- Promptly identify and isolate patients with possible COVID-19 and inform the correct facility staff and public health authorities
- Care for a limited number of patients with confirmed or suspected COVID-19 as part of routine operations
- Potentially care for a larger number of patients in the context of an escalating outbreak
- Monitor and manage any healthcare personnel that might be exposed to COVID-19
- Communicate effectively within the facility and plan for appropriate external communication related to COVID-19

The following checklist does not describe mandatory requirements or standards; rather, it highlights important areas for hospitals to review in preparation for potential arrivals of COVID-19 patients.

Elements to be assessed

1. Infection prevention and control policies and training for healthcare personnel (HCP):

- Facility leadership including the Chief Medical Officer, quality officers, hospital epidemiologist, and heads of services (e.g., infection control, emergency department, environmental services, pediatrics, critical care) has reviewed the Centers for Disease Control and Prevention's COVID-19 guidance.
<https://www.cdc.gov/coronavirus/2019-nCoV/guidance-hcp.html> ☐
- Facility provides education and job-specific training to HCP regarding COVID-19 including: ☐
 - Signs and symptoms of infection
 - How to safely collect a specimen
 - Correct infection control practices and personal protective equipment (PPE) use
 - Triage procedures including patient placement
 - HCP sick leave policies and recommended actions for unprotected exposures (e.g., not using recommended PPE, an unrecognized infectious patient contact)
 - How and to whom COVID-19 cases should be reported

<https://www.cdc.gov/coronavirus/2019-ncov/downloads/hospital-preparedness-checklist.pdf>

2. Process for rapidly identifying and isolating patients with confirmed or suspected COVID-19:

- Signs are posted at entrances with instructions to individuals with symptoms of respiratory infection to: immediately put on a mask and keep it on during their assessment, cover their mouth/nose when coughing or sneezing, use and dispose of tissues, and perform hand hygiene after contact with respiratory secretions. ☐
- Facemasks are provided to coughing patients and other symptomatic individuals upon entry to the facility. ☐
- Signs are posted in triage areas (e.g., ED entrances) advising patients with fever or symptoms of respiratory infection and recent travel outside the US, specifically to China, to immediately notify triage personnel so appropriate precautions can be put in place. ☐
- Alcohol based hand sanitizer for hand hygiene is available at each entrance and in all common areas. ☐
- Facility provides tissues and no-touch receptacles for disposal of tissues in waiting rooms and in common areas. ☐
- Facility has a separate well-ventilated space that allows waiting patients to be separated by 6 or more feet, with easy access to respiratory hygiene and cough etiquette supplies. ☐
- Facility has a process to ensure patients with confirmed or suspected COVID-19 are rapidly moved to an Airborne Infection Isolation Room (AIIR). ☐
- Alternatively, for patients that cannot be immediately placed in a room for further evaluation, a system is provided that allows them to wait in a personal vehicle or outside the facility (if medically appropriate) and be notified by phone or other remote methods when it is their turn to be evaluated. ☐
- Triage personnel are trained on appropriate processes (e.g., questions to ask and actions to take) to rapidly identify and isolate suspect cases. ☐
- Facility has a process that occurs after a suspect case is identified to include immediate notification of facility leadership/infection control. ☐
- Facility has a process to notify local or state health department of a suspect case soon after arrival. ☐
- Facility has a process for receiving suspect cases arriving by ambulance. ☐

3. Patient placement:

- Confirm the number and location of Airborne Infection Isolation Rooms (AIIRs) available in the facility (ideally AIIRs will be available in the emergency department and on inpatient units) ☐
- Document that each AIIR has been tested and is effective (e.g., sufficient air exchanges, negative pressure, exhaust handling) within the last month. The AIIR should be checked for negative pressure before occupancy. ☐

continue on next page

cont.

- Verify each AIIR meets the following criteria:
 - Minimum of 6 air changes per hour (12 air changes per hour are recommended for new construction or renovation).
 - Air from these rooms should be exhausted directly to the outside or be filtered through a high-efficiency particulate air (HEPA) filter before recirculation.
 - Room doors should be kept closed except when entering or leaving the room, and entry and exit should be minimized.
 - When occupied by a patient, the AIIR is checked daily for negative pressure.
- A protocol is established, which specifies that aerosol-generating procedures that are likely to induce coughing (e.g., sputum induction, open suctioning of airways) are to be performed in an AIIR using appropriate PPE.
- Facility has plans to minimize the number of HCP who enter the room. Only essential personnel enter the AIIR. Facilities should consider caring for these patients with dedicated HCP to minimize risk of transmission and exposure to other patients and HCP.
- Facility has a process (e.g., a log, electronic tracking) for documenting HCP entering and exiting the patient room.
- Facility has policies for dedicating noncritical patient-care equipment to the patient.

4. Transmission-Based Precautions (use Standard, Contact, Airborne Precautions plus eye protection for patients with confirmed or suspected COVID-19 cases):

- Personal protective equipment (PPE) and other infection prevention and control supplies (e.g., hand hygiene supplies) that would be used for both healthcare personnel (HCP) protection and source control for infected patients (e.g., facemask on the patient) are located in sufficient supply including at patient arrival, triage, and assessment locations.
- Facility has a respiratory protection program. Appropriate HCP have been medically cleared, fit-tested, and trained for respirator use.
- HCP receive appropriate training, including "just in time" training on selection and proper use of (including putting on and removing) PPE, with a required demonstration of competency.
- Facility has a process for auditing adherence to recommended PPE use by HCP.

5. Movement of patients with confirmed or suspected COVID-19 within the facility:

- Patient movement outside of the AIIR will be limited to medically-essential purposes.
- A protocol is in place to ensure that, if the patient is being transported outside of the room, HCP in the receiving area are notified in advance.
- Patients transported outside of their AIIR will be asked to wear a facemask and be covered with a clean sheet during transport.

6. Hand hygiene (HH):

- HH supplies, including alcohol-based hand sanitizer are readily accessible in patient care areas, including areas where HCP remove PPE. ☐
- Facility has a process for auditing adherence to recommended hand hygiene practices by HCP. ☐

7. Environmental cleaning:

- Facility has a plan to ensure proper cleaning and disinfection of environmental surfaces and equipment in the patient room. ☐
- If environmental services personnel are given this responsibility, they should be appropriately trained and fit-tested. ☐
- All HCP with cleaning responsibilities understand the contact time for selected products. ☐
- Facility has a process to ensure shared or non-dedicated equipment is cleaned and disinfected after use according to manufacturer's recommendations. ☐
- Facility uses an EPA-registered hospital-grade disinfectant with EPA-approved emerging viral pathogens claims on hard non-porous surfaces. ☐
 - If there are no available EPA-registered products that have an approved emerging viral pathogen claim for COVID-19, products with label claims against human coronaviruses should be used according to label instructions.

8. Monitoring and managing HCP:

- The facility follows the local/state public health authority's policies and procedures for monitoring and managing HCP with potential for exposure to COVID-19, including ensuring that HCP have ready access, including via telephone, to medical consultation. ☐
- Facility has a process to track exposures and conduct active- and/or self-monitoring of HCP if required by public health. ☐
- Facility has a process to conduct symptom and temperature checks prior to the start of any shift of asymptomatic, exposed HCP that are not work restricted. ☐

9. Visitor access and movement within the facility:

- Plans for visitor access and movement within the facility have been reviewed and updated within the last 12 months.
- Visitors are screened for symptoms of acute respiratory illness before entering the hospital.
- Facility has a plan to restrict visitation to rooms of patients with confirmed or suspected COVID-19.
- If visitors are allowed to enter the room of a confirmed or suspected COVID-19 patient, the facility will:
 - Enact a policy defining what PPE should be used by visitors.
 - Provide instruction to visitors before they enter a patient room, on hand hygiene, limiting surfaces touched, and use of PPE according to current facility policy.
 - Maintain a record (e.g., a log with contact information) of all visitors who enter and exit the room.
 - Ensure that visitors limit their movement within facility (e.g. avoid the cafeteria).

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10. Facility regularly monitors the situation on CDC's coronavirus disease (COVID-19) web page. www.cdc.gov/COVID19

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Thank You

- DeSimone.Daniel@mayo.edu

- Twitter: @DeSimoneDaniel

