

Management of Patients with Human Immunodeficiency Virus (HIV) in the Intensive Care Unit (ICU)

A presentation for HealthTrust Members
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Speaker Disclosures

- * The presenter and their preceptor have no financial relationships with any commercial interests pertinent to this presentation.
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Objectives

1. Identify the challenges with continuing antiretroviral therapy in patients admitted to the ICU.
2. Recall toxicities and drug interactions of common antiretroviral medications that may affect the care of critically ill patients with HIV.
3. Recognize appropriate screening and treatment of opportunistic infections that may present in patients with HIV.

Current State of HIV Treatment

Background History of HIV

HIV

First Diagnosed in 1981

Attacks immune system by destroying CD4+ T cells which leaves patients vulnerable to serious infections

75 million people have become infected with HIV

32 million people have died from AIDS (acquired immunodeficiency syndrome)-related illness

Sources: HIV Historical Timeline. hivhistory.org.

National Institute of Allergy and Infectious Diseases. Nih.gov.

Centers for Disease Control and Prevention. *HIV Surveillance Supplemental Report*. 2021.

Background History of HIV

Stages of HIV Infection

- Transmission
 - Sexual intercourse, exposure to infected blood, or perinatal transmission
- Acute HIV Infection
 - First 6 months after transmission
 - Up to 60% asymptomatic

Progression to AIDS

- Definition:
 - CD4 count of < 200 cells/microL
 - Presence of AIDS-defining illness
- AIDS diagnosed ~ 8 – 10 years without use of antiretroviral therapy (ART)
- After AIDS Diagnosis without ART
 - Median survival ~ 12 – 18 months

Sources: National Institute of Allergy and Infectious Diseases. Nih.gov.

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV.

Antiretroviral Therapy (ART)

Goals of treatment:

1. Prevent HIV-associated morbidity and mortality
2. Achieve and maintain a HIV-1 RNA below detectable levels

When to start treatment:

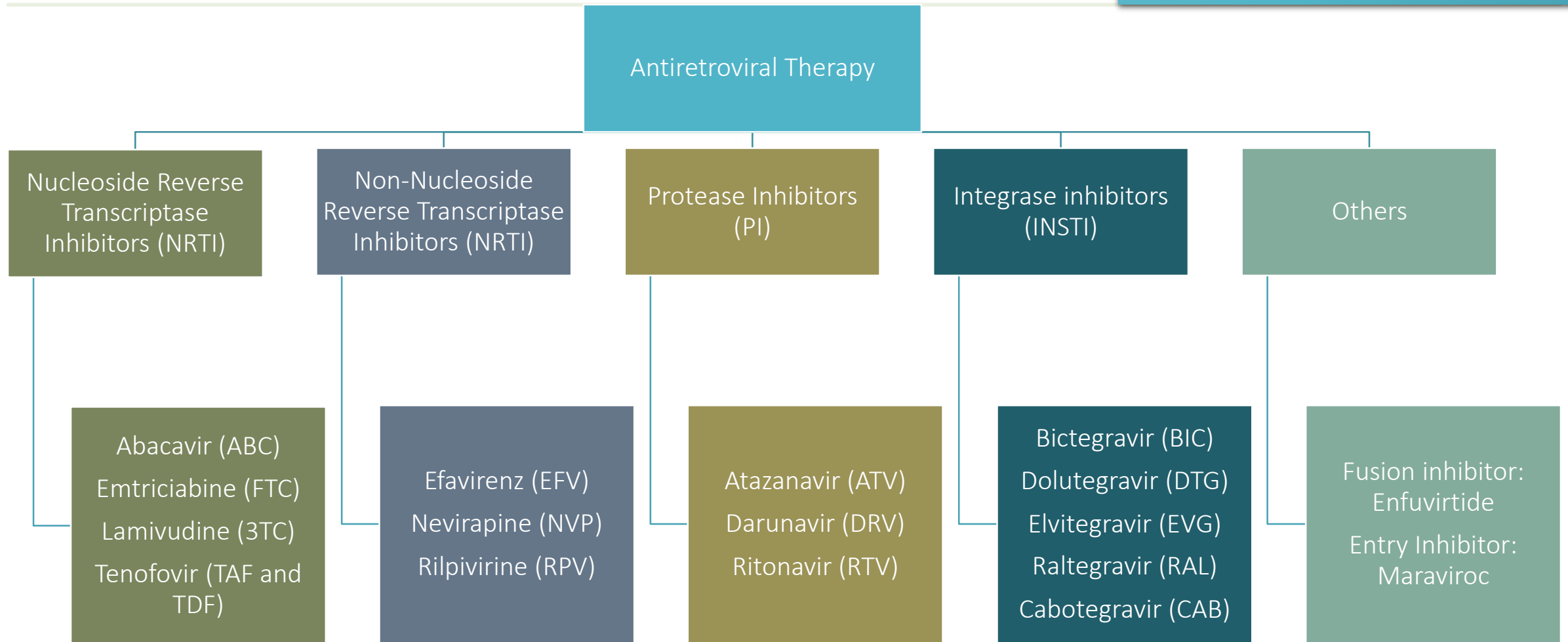
- Immediately (or as soon as possible) following diagnosis

Starting regimen for treatment-naive patients:

- Typically a 3 drug regimen

HIV Treatments: Examples

Typical starting regimen:
2 NRTI plus 1 INSTI



Prognosis

~1.2 million people in the United States are living with HIV

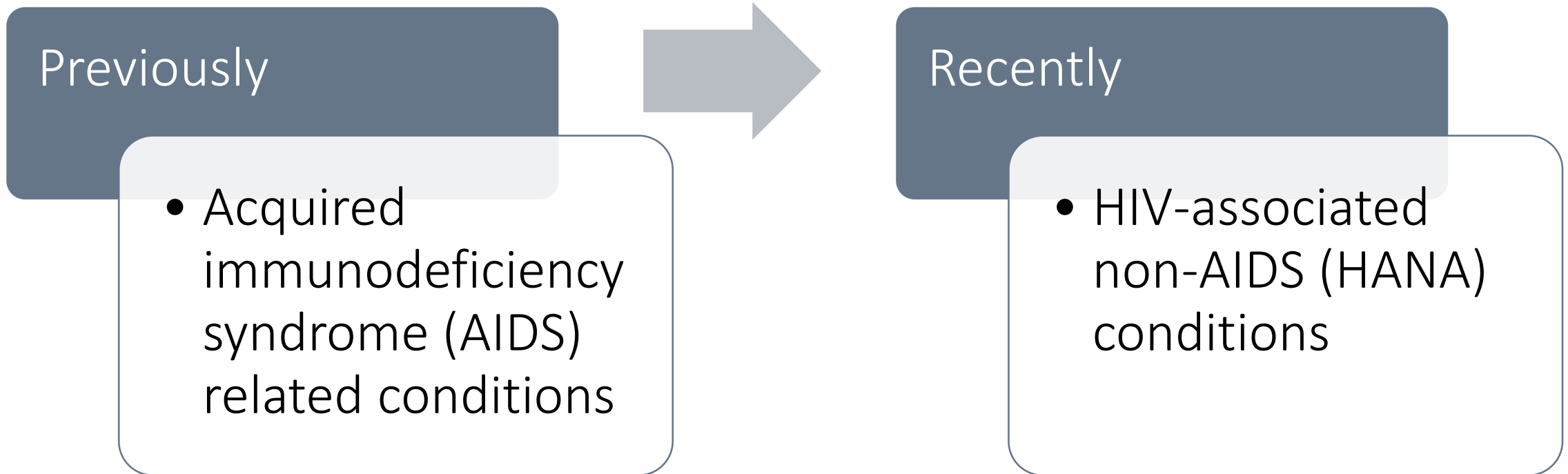
- ~ 56.8% have well-controlled disease with ART (undetectable levels of HIV RNA)

HIV care from inpatient setting → outpatient setting

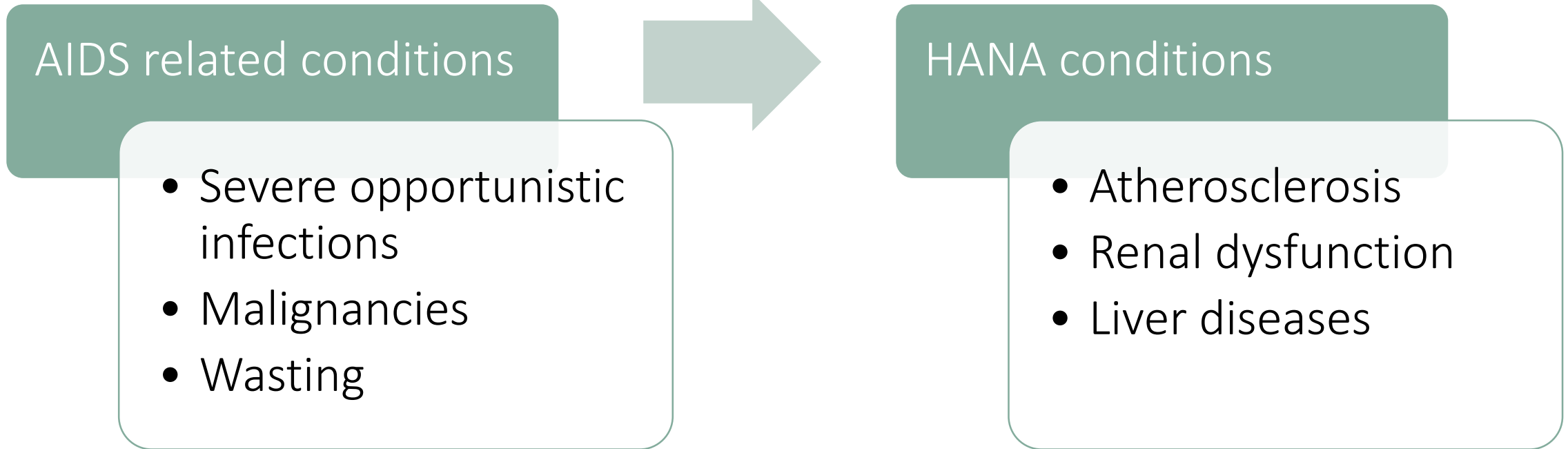
Patient Population

- Older, more comorbid conditions, increased exposure to ART

Critical Care Admissions in Patients with HIV



Critical Care Admissions in Patients with HIV



Other Risks for Patients with HIV

Increased Risk for Critical Illness

Advancing
Age

Comorbid
Conditions

Opportunistic
and Severe
Infections

Adverse
Effects from
ART

HIV Med Errors in the Inpatient Setting

2014
Review
of 25
Studies

86% incidence of Med Errors for HIV therapies

27 – 72% of errors occurred on admission

Protease inhibitors were related to the largest percentage of drug errors

HIV Med Errors in the Inpatient Setting

Types of
Errors
Discovered
in Review

ART Omission/
Incomplete Regimen

As high as 69.2% in one study

Another study showed that 43% of patients received an incomplete regimen

Dosing Errors

Dose scheduling errors (2.5% to 37%)

Under dosing (6.6% to 48.1%)

Overdosing (5.9% to 34.2%)

Renal and/or hepatic failure (7% to 29.5%)

Drug Interactions

How do we care for critically ill patients who have HIV?

Treatment Considerations for Patients with HIV in the ICU

Continuation of ART

Drug Interactions with ART

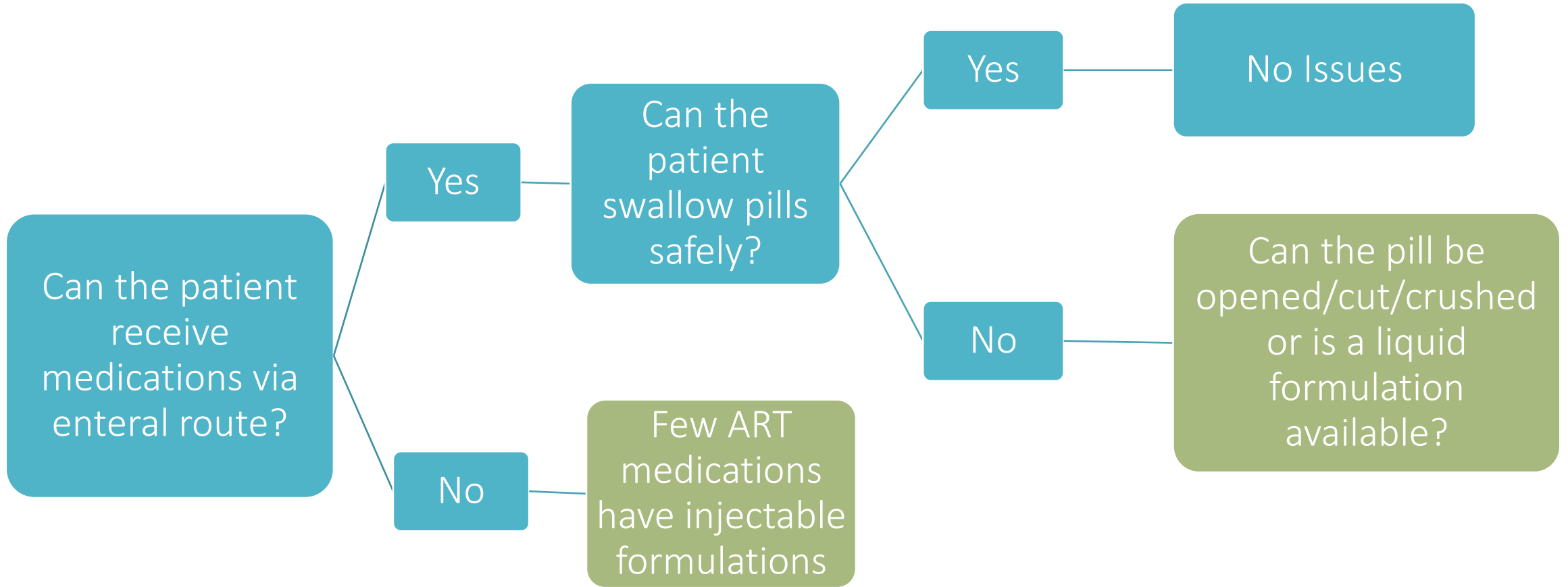
Adverse Drug Reactions with ART

Opportunistic Infections

Continuation of ART

- Recommended to continue ART whenever possible
Decreases the risk for HIV resistance mutations due to interruptions
- Considerations for continuing ART in critically ill patients
 - Medication delivery (PO vs NG vs IV)*
 - Renal impairment*
 - Hepatic impairment*
 - Drug Interactions*
 - Adverse drug reactions related to ART*

Medication Delivery Issues



Medication Delivery Issues: Examples

ART THAT HAVE INJECTABLE FORMULATIONS

IV

- Zidovudine
- Rilpivirine

SubQ/IM

- Enfuvirtide
- Cabotegravir
- Rilpivirine

ART THAT HAVE LIQUID OR CRUSHABLE FORMULATIONS

Liquid

- Abacavir
- Emtricitabine
- Lamivudine
- Nevirapine
- Raltegravir
- Darunavir

Crushable

- Emtricitabine
- Lamivudine
- Tenofovir
- Efavirenz
- Raltegravir
- Dolutegravir

Medication Delivery Issues

Do we have access to these formulations?

Administration of ART

Option 1: Continue current ART Regimen

- Can be broken up into individual medications if needed
- Can have patient bring in home medication

Option 2: Hold entire regimen short term (< 2 weeks)

- May be considered if current ART regimen cannot be continued
- Still has risk of inducing resistance

Option 3: Administer partial regimen

- LAST LINE option
- Risk inducing resistance

Assessment Question #1

A patient with HIV is admitted to the ICU following a car accident and now has enteral access through a nasogastric tube. He takes bicitgravir/emtricitabine/tenofovir (BIC/FTC/TAF, Biktarvy®) as his home antiretroviral therapy. When should his BIC/FTC/TAF be restarted following admission?

- A. When he is transferred out of the ICU
- B. When he is discharged
- C. As soon as 1 of the 3 active medications is able to be administered
- D. As soon as all 3 active medications are able to be administered

Assessment Question #1:

Correct Response

A patient with HIV is admitted to the ICU following a car accident and now has enteral access through a nasogastric tube. He takes bicitgravir/emtricitabine/tenofovir (BIC/FTC/TAF, Biktarvy®) as his home antiretroviral therapy. When should his BIC/FTC/TAF be restarted following admission?

- A. When he is transferred out of the ICU
- B. When he is discharged
- C. As soon as 1 of the 3 active medications is able to be administered
- D. As soon as all 3 active medications are able to be administered**

Drug Interactions with ART

Extremely common with many antiretroviral medications

Must be evaluated with the start of any new medication

- Especially important for interactions that may increase metabolism of ART

Protease inhibitors and non-nucleoside reverse transcriptase inhibitors

- All metabolized by CYP enzymes (3A4 and others)

Drug Interactions with ART

Cobicistat and ritonavir

- 3A4 inhibitors
- Contraindicated interactions:
 - Amiodarone, phenobarbital, rivaroxaban, oral midazolam etc.

Integrase inhibitors

- Chelate with polyvalent cations
- Interactions: calcium, iron, magnesium, zinc

Tenofovir alafenamide

- Metabolized via P-glycoprotein
- Contraindicated with strong P-glycoprotein inducers
 - Carbamazepine, oxcarbazepine, phenobarbital, and phenytoin

Drug Interactions with ART

Fluconazole (azole antifungals)

- Strong CYP 2C19 inhibitor, moderate CYP 2C9 and 3A4 inhibitor
- Increase levels of many ART meds
- Others can increase levels of azole antifungals

Antacids

- Some ART medications require acidic environments for proper absorption
 - Examples: atazanavir and rilpivirine
- Avoid agents that may raise the gastric pH

Resources for ART Drug Interactions



HIV Drug Interactions



UNIVERSITY OF
LIVERPOOL

www.hiv-druginteractions.org



www.clinicalinfo.hiv.gov

Other General Hospital
approved Drug Information
Resources

Assessment Question #2

The previously mentioned patient was diagnosed with a TBI as a result of the car accident and is requiring seizure prophylaxis while he recovers from his accident. What antiepileptic would NOT interact with his BIC/FTC/TAF?

- A. levetiracetam
- B. phenobarbital
- C. phenytoin
- D. carbamazepine

Assessment Question #2: Correct Response

The previously mentioned patient was diagnosed with a TBI as a result of the car accident and is requiring seizure prophylaxis while he recovers from his accident. What antiepileptic would NOT interact with his BIC/FTC/TAF?

A. levetiracetam

B. phenobarbital

C. phenytoin

D. carbamazepine

Adverse Drug Reactions Related to ART

Many ART medications have related adverse effects and/or toxicities

Up to 6% of ICU admission for HIV patients related to ART toxicity

More severe with older HIV therapies

Some can be prevented

HLA-B*5701 testing for abacavir

Dose adjustments for renal function

Identification of drug interactions

Adverse Drug Reactions Related to ART

Adverse Effect	ART Associated with Reaction
Decreased Bone Density	Tenofovir disoproxil fumarate
QTc Prolongation	Rilpivirine, efavirenz
Cardiovascular Disease ** Dyslipidemia	Abacavir, darunavir, lopinavir/ritonavir ** Tenofovir alafenamide, efavirenz, elvitegravir, boosted PI
Lactic Acidosis	Older NRTIs (stavudine, didanosine, zidovudine)
Myopathies	Raltegravir and dolutegravir
Renal Impairment	Tenofovir disoproxil fumarate, atazanavir, lopinavir/ritonavir

Adverse Effects from Renal Impairment

ART Medication that Requires Renal Adjustment	Dose Adjustment
Emtricitabine	Dose Adjust with CrCl <50 mL/min
Lamivudine	Dose Adjust with CrCl <30 mL/min
Tenofovir Alafenamide	AVOID in CrCl <15
Tenofovir Disoproxil Fumarate	Dose Adjust with CrCl <50 mL/min
** Combination products may have different CrCl limits but all combination products that contain one of these ingredients will have some renal adjustment	

CrCl: Creatinine Clearance

Sources: Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV.
Barbier F, Mer M, Szychowiak P, et al. *Intensive Care Med.* 2020.

Opportunistic Infections (OI)

Patients with low CD4 counts and high HIV viral loads are at increased risk for opportunistic infections

Typically present as acute respiratory failure (ARF) or neurological disorders

ICU patients with HIV are also at an increased risk for hospital acquired infections

Including: hospital acquired pneumonia, ventilator associated pneumonia, catheter associated bloodstream infections, etc.

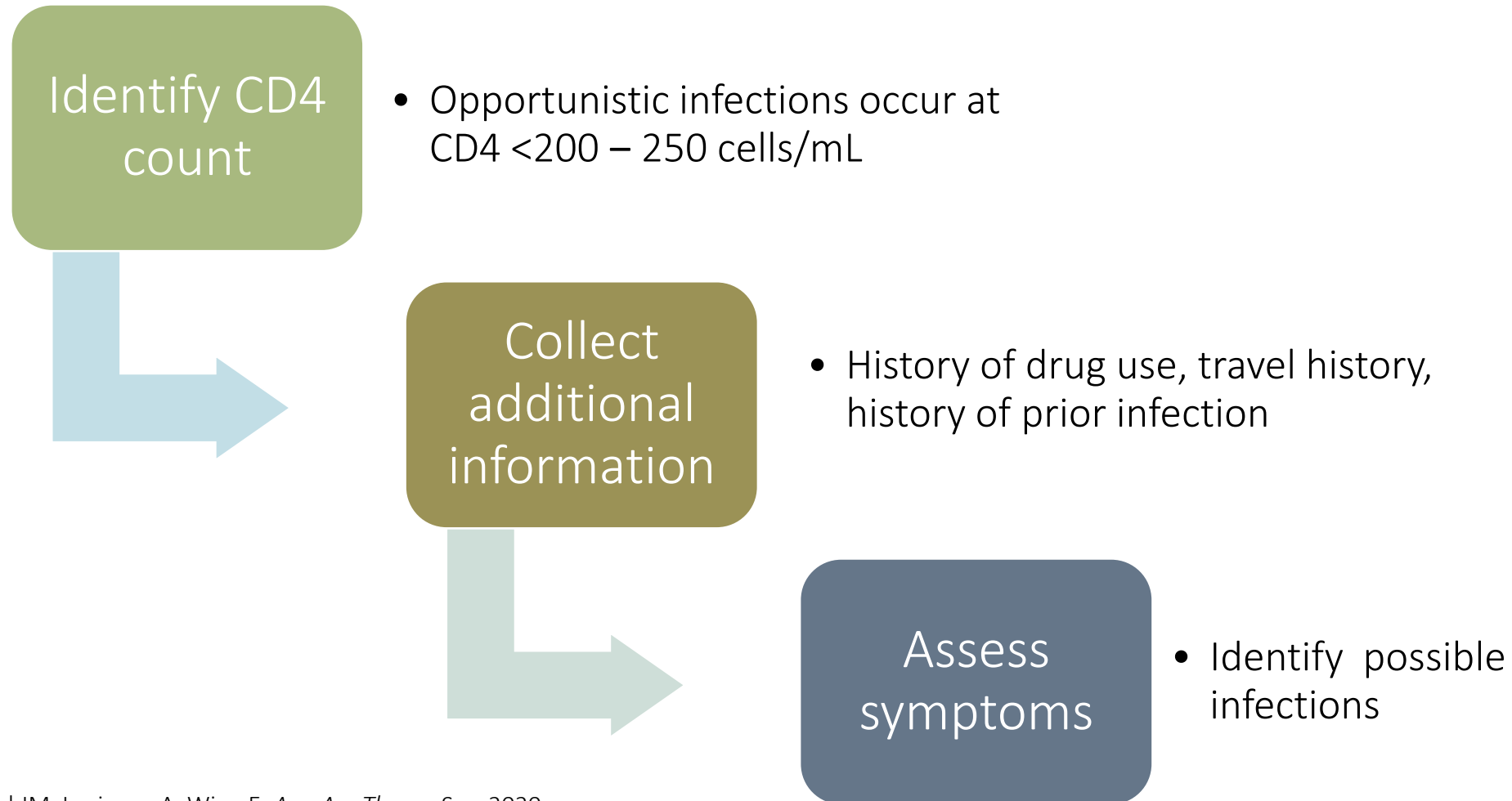
Sources: Azoulay É, de Castro N, Barbier F. *Chest*. 2020

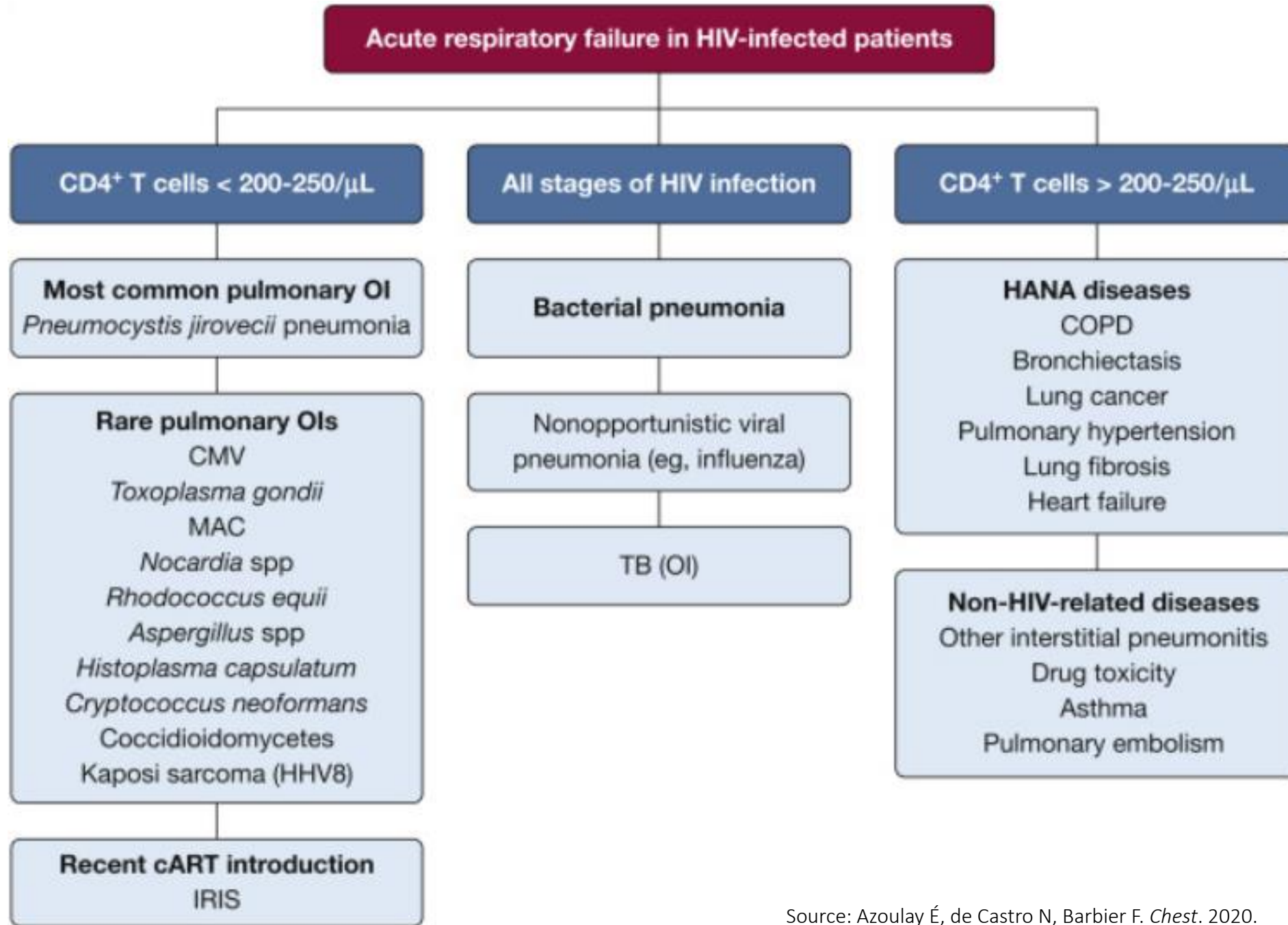
Garland JM, Levinson A, Wing E. *Ann Am Thorac Soc*. 2020.

Barbier F, Mer M, Szychowiak P, et al. *Intensive Care Med*. 2020.

Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV.

OI: Approach to Treatment





Abbreviations

CMV:
Cytomegalovirus

MAC:
Mycobacterium avium Complex

IRIS:
Immune reconstitution inflammatory syndrome

TB:
Tuberculosis

cART: combination antiretroviral therapy

OI: *Pneumocystis jiroveci* (PCP)

Background

Incidence Rates and Prognosis

- 10% to 20% of acute respiratory failure (Declining)
- 1/3 of AIDS related PCP diagnoses result in ICU management

Diagnosis

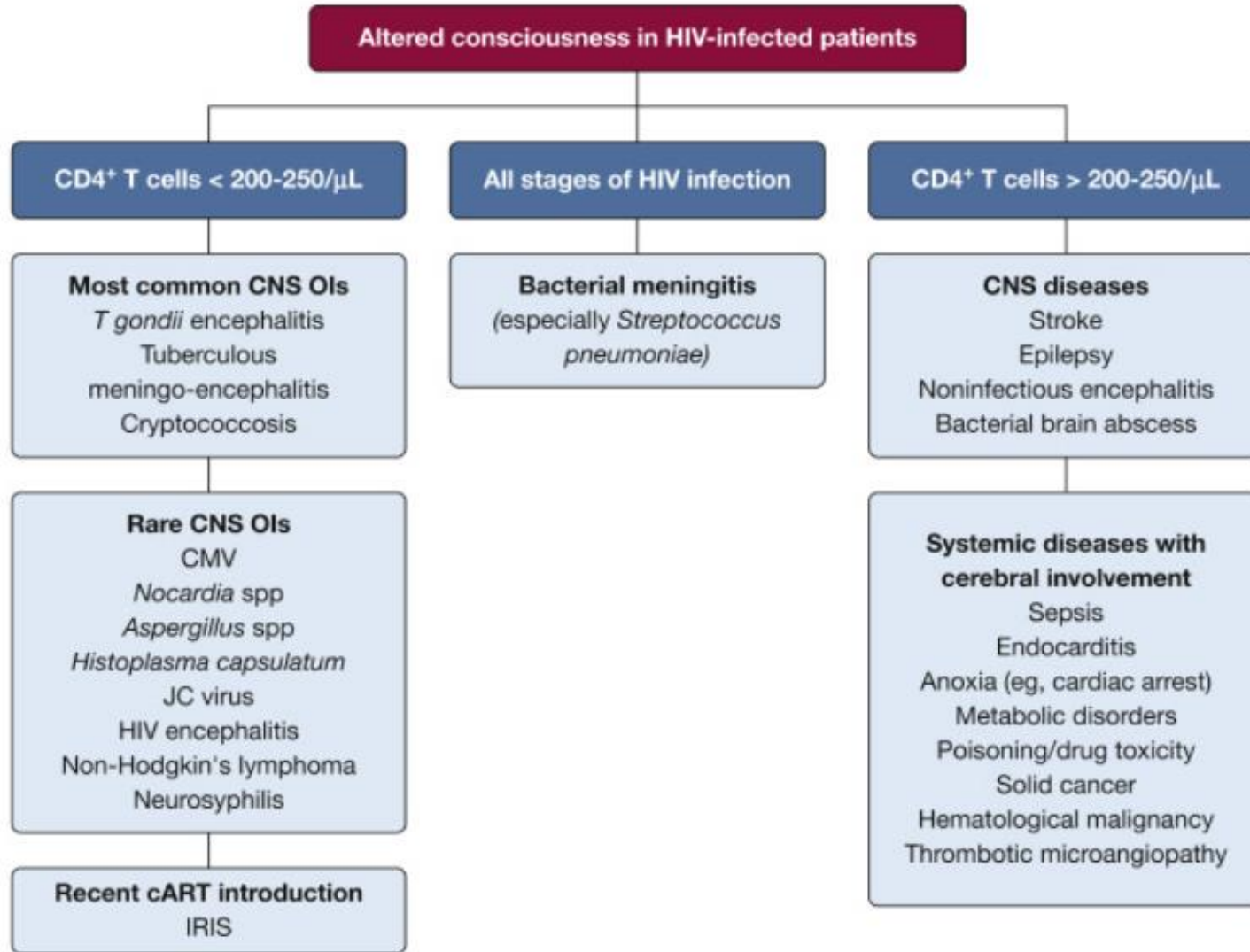
Multifactorial

- Bronchoscopy (alternative: sputum testing)
- β - D- glucan test

Treatment

Antibiotics and Corticosteroids

- Sulfamethoxazole (SMX) – Trimethoprim (TMP): TMP 15 – 20 mg and SMX 75 – 100 mg (PO or IV)
- Prednisone taper if
 - PaO₂ < 70 mmHg on room air or Alveolar-arterial DO₂ gradient > 35 mmHg



Abbreviations

CMV:
Cytomegalovirus

IRIS:
Immune reconstitution inflammatory syndrome

Opportunistic Infections (OI)

Infection	CD4 threshold for consideration	Primary Treatment
<i>Pneumocystis jiroveci</i> (PCP)	<200 cells/mL	Sulfamethoxazole - trimethoprim
Tuberculosis	<200 cells/mL	Isoniazid+rifampin +pyrazinamide+ethambutol
<i>Histoplasma capsulatum</i>	< 100 cells/mL	Liposomal amphotericin B and itraconazole
<i>Toxoplasma gondii</i>	< 100 cells/mL	Pyrimethamine
<i>Cryptococcus neoformans</i>	< 100 cells/mL	Liposomal amphotericin B and flucytosine
<i>Mycobacterium avium</i> Complex (MAC)	< 50 cells/mL	Clarithromycin + ethambutol
Cytomegalovirus (CMV)	< 50 cells/mL	Ganciclovir or valganciclovir

Sources: Garland JM, Levinson A, Wing E. *Ann Am Thorac Soc*. 2020.

Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV.

Assessment Question #3

In the first 24 hours of admission, the previous patient also shows signs of pneumonia. What organism may be the cause of pneumonia in this patient?

(Note: patient has a CD4 count of 145)

- A. *Pneumocystis jiroveci*
- B. *Streptococcus pneumoniae*
- C. *Haemophilus influenza*
- D. All of the above

Assessment Question #3:

Correct Response

In the first 24 hours of admission, the previous patient also shows signs of pneumonia. What organism may be the cause of pneumonia in this patient?

(Note: patient has a CD4 count of 145)

- A. *Pneumocystis jiroveci*
- B. *Streptococcus pneumoniae*
- C. *Haemophilus influenza*
- D. All of the above

Other Considerations



Previous studies in critical care may have excluded patients with HIV

May have social factors that may impact care

Continue to follow HIPAA and confidentiality with HIV diagnosis

Future Improvements in Inpatient Care of Patients with HIV

Practice Improvement: Antiretroviral Stewardship

Supported by

The Infectious Diseases Society of America (IDSA)

HIV Medicine Association (HIVMA)

American Academy of HIV Medicine (AAHIVM)

Defined as:

“coordinated interventions designed to improve continuity of care for patients receiving ARTs through the utilization of evidence-based ART practices including medication reconciliation, dosing, mitigation of drug interactions, and prevention of viral resistance.”

Antiretroviral Stewardship Components

Collaborating with
physicians and
other healthcare
providers

Tracking and
reporting
utilization of ART

Completing
accurate
medication
reconciliation

Assisting in
transitions of care

Education of other
healthcare learners

Approaches and Strategies for Antiretroviral Stewardship Programs

1. Checklists to ensure safe prescribing practices
2. Computerized Providers Order Entry sets
3. Prospective review strategies for patients with HIV on admission and at discharge

Study Demonstrating a Pharmacist Impact on Decreasing Medication Errors

Design

- Population:
 - HIV-infected hospitalized patients who had been prescribed ART in the outpatient setting
- Location:
 - 695-bed urban, academic institution
- Intervention:
 - Chart review preformed by a pharmacy resident within 72 hours of admission

A Pharmacist Impact on Decreasing Medication Errors: Results

Population and Error Rates

- 86 patients with HIV on ART admitted to the hospital
- 54.7% of patients had at least 1 medication error on admission

Pharmacist Review

- Reduction in correctable errors by 89.9%
- Pharmacist intervention reduced duration of error from 3.5 days to less than 1 day

Impact on Care

- 90% acceptance rate of pharmacists' recommendations
- Time allotted to this task: 18.5 minutes per patient

Benefits of Antiretroviral Stewardship

Reduction in
Medication
Errors

Prevention of
Resistance

Enhanced
Clinical
Outcomes

Summary

Due to the advances in HIV treatment, patients with HIV often are admitted to the ICU for similar reasons as patients without HIV.

Patients with HIV should be evaluated for continuation of their ART regimen, ART toxicities, ART drug interactions, and risk of opportunistic infections

Antiretroviral stewardship should be implemented into critical care and inpatient practices to reduce medication errors and limit mutations for patients with HIV.

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Thank you!

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