
Opioids and Opiates

Environmental and nutritional pathology

Toxicologic injury • organ pathology • clinicopathologic interpretation

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Learning objectives

Distinguish naturally occurring opiates from the broader opioid group.

Explain how potency, adulteration and loss of tolerance increase overdose risk.

Connect heroin exposure with pulmonary, infectious, cutaneous and renal pathology.

Interpret representative multisystem clinicopathologic scenarios.

Drug injury has more than one mechanism

Pharmacologic action

Direct CNS and respiratory drug effects

Adulterants / contaminants

Particulate and toxic admixture reactions

Hypersensitivity

Reaction to the drug or its additives

Contaminated needles

Infections arising from injection exposure

Opiates and opioids: Terminology

Opiates

Naturally occurring chemicals derived from poppy plants

Morphine is the naturally occurring example

Opioids

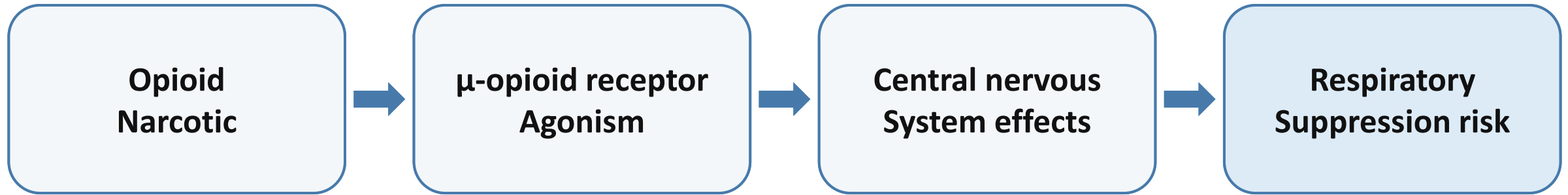
Broader group including derivatives and synthetic variants

Includes agents used medically and outside therapeutic settings

Opioid agents and their exposure contexts

Agent	Context in the chapter
Morphine	Example of a naturally occurring opiate
Heroin	Poppy-derived street drug related to morphine
Oxycodone / hydrocodone	Prescription opioids also used nontherapeutically
Tramadol / methadone	Prescription opioids also used nontherapeutically
Fentanyl	Highly potent synthetic opioid; also a therapeutic analgesic

The μ -opioid receptor is a molecular target



Schematic

Central effects include somnolence and sedation; Profound respiratory suppression is the major acute danger.

Therapeutic efficacy does not imply safety in misuse

Medical use

Fentanyl is an effective sedative and analgesic when appropriately used

Supervised administration provides clinical oversight

Nontherapeutic use

Unknown drug composition and tolerance status

Potentially fatal respiratory suppression

Global exposure: Historical figures

31.5 million

Opiate users

60.4 million

Opioid users

Global estimates for 2021 (UNODC 2023). Groups may overlap and should not be added together.

Opioid overdose: Historical public-health context

Illicit synthetic opioids, particularly fentanyl, increased the burden of drug overdose.

The text reports more than 80,000 U.S. Opioid-related deaths in 2023.

Mixing or substitution with fentanyl can make the actual exposure unpredictable.

The figure describes 2023; It is not a present-day surveillance count.

Four broad routes to heroin-associated harm

Direct drug effect

Central nervous system and respiratory depression

Cutting agents

Foreign-body and other toxic reactions

Hypersensitivity

Reactions to heroin or its adulterants

Contaminated needles

Infection at local and distant sites

Fentanyl amplifies drug-composition uncertainty

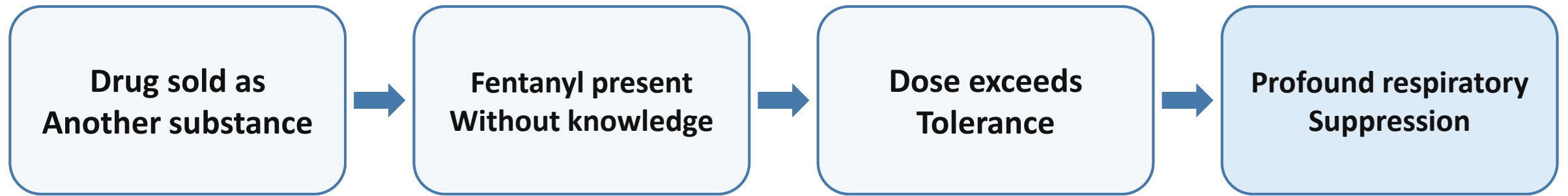
Fentanyl is highly potent and inexpensive to produce illicitly.

It may be mixed with, or substituted for, another drug.

The person taking the drug may not know fentanyl is present.

Unexpected potency magnifies overdose risk, especially without opioid tolerance.

Concealed fentanyl exposure: Causal sequence



Schematic

Schematic: The absence of knowledge and tolerance can convert exposure into an acute lethal event.

Tolerance modifies overdose risk

Tolerance present

Repeated exposure may establish tolerance

No guarantee of protection from a very potent
or variable illicit supply

Tolerance absent or lost

Unfamiliar users may be particularly
vulnerable

Risk also rises when former tolerance has
waned

Neurobehavioral effects described for heroin

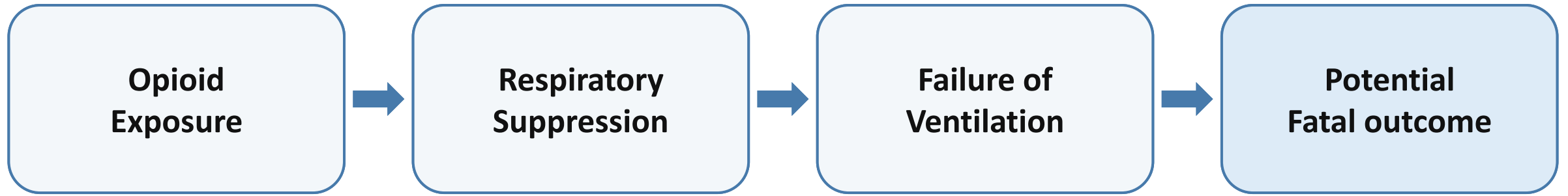
Euphoria is one recognized central nervous system effect.

Hallucinations may occur.

Somnolence and sedation reflect prominent CNS suppression.

The clinical effects vary; No single behavioral finding proves exposure.

Fatal opioid toxicity centers on breathing



Schematic

Respiratory depression is the usual mechanism of death described in the chapter.

Naloxone reverses opioid effects when timely

Naloxone is an opioid antagonist.

It can rapidly reverse opioid-induced respiratory suppression.

The opportunity for reversal is time-sensitive.

Antagonist reversal addresses pharmacologic toxicity, not injection-associated infections.

Why unsuspected users face disproportionate danger

Content

An unrecognized potent synthetic opioid

Potency

Profound effect from unexpected exposure

Tolerance

Little or no prior opioid adaptation

Outcome

Rapid respiratory suppression

Heroin: Origin and clinical setting

Heroin is a poppy-derived street drug closely related to morphine.

The sold product is generally diluted with one or more cutting agents.

The amount of active drug is often unknown to the purchaser.

Intravenous and subcutaneous exposure create additional route-associated injury.

Administration routes shape tissue injury

Intravenous injection

Immediate entry into blood circulation

Exposure to contaminated equipment

Vein injury with repeated injection

Subcutaneous injection

Local deposition in skin/subcutis

Cellulitis, abscess or ulceration

Repeated local damage and scarring

Cutting agents are a second toxic exposure

The heroin supply may contain talc or quinine.

Talc is linked with foreign-body granulomatous lesions.

Quinine itself has neurologic, renal and auditory toxicity.

Reactions may arise from the admixture rather than heroin alone.

Variable street purity limits dose prediction

2%–90%

Purity range described in chapter

Unknown

Active dose to purchaser

The reported range is a source-era observation, not a universal or current purity distribution.

Independent sources of dose uncertainty

Variable purity

Active heroin proportion differs between illicit preparations

Unknown dose

Purchased quantity does not establish opioid amount

Fentanyl admixture

A more potent opioid may be added without knowledge

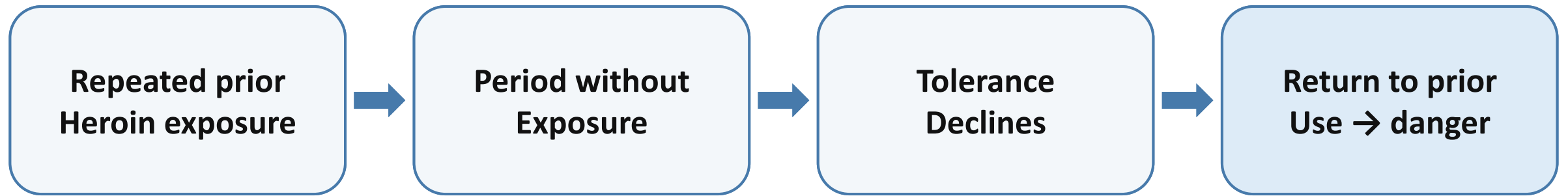
Tolerability

Tolerance does not reliably match unknown drug potency

Immediate death has several mechanisms

Potential terminal event	Reported pathology / effect
Respiratory depression	Profound suppression of breathing
Arrhythmia	Potential lethal disturbance of cardiac rhythm
Cardiac arrest	Final cessation of cardiac function
Severe pulmonary edema	Acute lung fluid accumulation

Loss of tolerance explains deaths after abstinence



Schematic

Loss of tolerance during a period without drug exposure can make a return to use dangerous.

Respiratory depression is the primary toxic target

Respiratory suppression is a predictable pharmacologic effect of opioids.

In profound toxicity, it is the usual cause of death.

Potent synthetic opioids can rapidly intensify this effect.

Reversibility with naloxone demonstrates the importance of recognizing the mechanism.

Cardiac events may also be terminal

Arrhythmia can contribute to sudden opioid-associated death.

Cardiac arrest is another reported terminal event.

An arrhythmia may culminate in cardiac arrest.

Neither an arrhythmia nor cardiac arrest identifies a unique myocardial lesion.

Severe pulmonary edema in sudden death

Pulmonary edema is explicitly linked to sudden heroin-associated death.

The amount of fluid accumulation may be clinically severe.

It belongs in the acute toxicologic differential rather than being assumed infectious.

Pulmonary edema and infectious lung injury are different etiologic categories.

Pulmonary disease is heterogeneous

Acute toxic injury

Pulmonary edema

Vascular infection

Septic pulmonary embolism from endocarditis

Parenchymal infection

Lung abscess / opportunistic infection

Particle reaction

Foreign-body granulomas from adulterants

Edema versus septic disease: Different pathways

Pulmonary edema

Associated with acute toxicity and sudden death

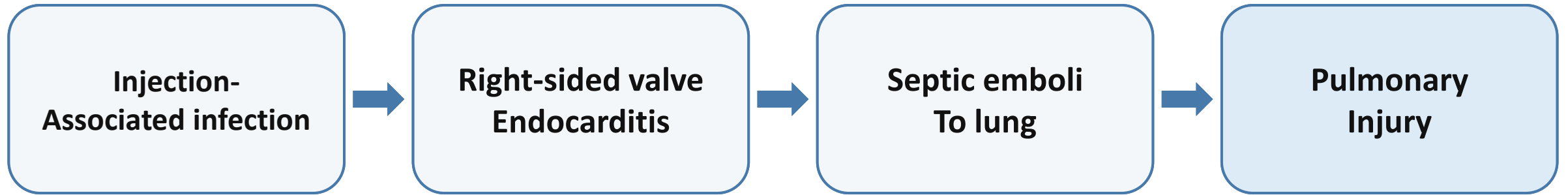
Fluid accumulation is the essential lesion

Septic embolic disease

Associated with infective endocarditis

Infected material can reach lung circulation

Right-sided endocarditis can injure the lung



Schematic

The vascular relationship helps explain why the tricuspid valve and lungs are linked clinically.

Lung abscess belongs to the infectious spectrum

Lung abscess is listed among heroin-associated pulmonary complications.

It must be distinguished conceptually from sterile pulmonary edema.

Septic embolization is another infectious pulmonary mechanism.

An abscess cannot be attributed to a particular pathogen from opioid exposure alone.

Opportunistic pulmonary infections

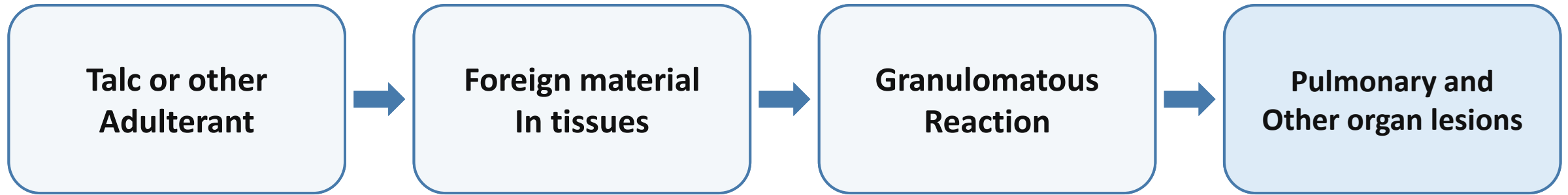
Opportunistic infections form part of the reported pulmonary spectrum.

They represent an infectious, not purely pharmacologic, injury category.

Associated HIV infection is another recognized hazard in people sharing injection equipment.

The infecting organism must be established by case-specific evidence.

Injected adulterants may trigger granulomas



Schematic

Schematic of particle-associated foreign-body inflammation; Not a photomicrograph.

Foreign-body giant cells are a morphologic clue

Talc crystals may be trapped within foreign-body granulomas.

Some crystals are enclosed by multinucleated foreign-body giant cells.

This finding favors a tissue reaction to exogenous particulate material.

It does not identify the active opioid or establish a drug concentration.

Polarization can reveal retained talc

Routine tissue assessment

Recognize a foreign-body granulomatous pattern

Look for embedded particulate material

Polarized light

May highlight retained talc crystals

Can improve detection of material within giant cells

Granulomas are not restricted to the lungs

Pulmonary tissue is the principal site emphasized in the text.

Other described sites include spleen and liver.

Upper-extremity–draining lymph nodes may also contain foreign-body granulomas.

Distribution is consistent with systemic exposure to injected particulate adulterants.

Four pulmonary lesions require distinct explanations

Lesion	Dominant causal category	Discriminating idea
Edema	Acute toxic response	Fluid in lung
Septic emboli	Valve-related infection	Infected embolic material
Abscess / opportunistic infection	Infectious complication	Pulmonary infection
Talc granuloma	Foreign-body reaction	Particles and giant cells

Injection-associated infection is multisite

Skin / subcutis

Cellulitis, abscess and ulceration

Heart valves

Often right-sided, especially tricuspid

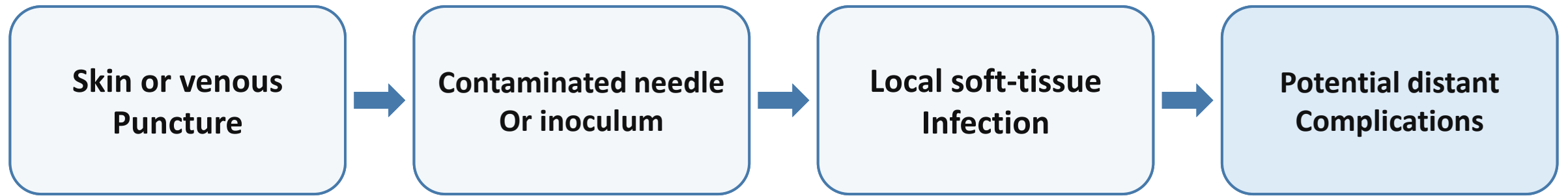
Liver

Viral hepatitis associated with needle sharing

Lungs

Septic emboli, abscess and other infections

Local injection sites can seed infection



Schematic

The diagram distinguishes entry site pathology from infection of valves or lung.

Tricuspid valve endocarditis is characteristic

Endocarditis is a recognized complication of injection-associated drug use.

Right-sided heart valves are often involved.

The tricuspid valve is highlighted as a particularly typical site.

In one hospitalized series, more than 10% had endocarditis; This is not a population prevalence.

Staphylococcus aureus is frequently implicated

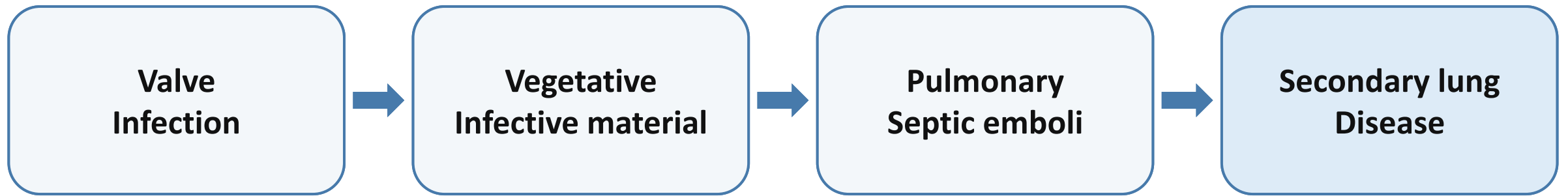
Staphylococcus aureus causes most cases of the endocarditis described in this setting.

Fungi are also implicated.

Many other organisms can cause the complication.

Organism identification requires patient-specific clinical microbiology, not source-level inference.

Valve and lung findings may be causally linked



Schematic

Anatomic schematic: Material from right-heart valves travels toward pulmonary vessels.

Sharing needles permits viral hepatitis transmission

Viral hepatitis is described as the most common infection in the addicted population under discussion.

Needle sharing is the identified exposure route.

A diagnosis of viral hepatitis does not by itself establish the infecting viral subtype.

Bloodborne viral infection is distinct from direct opioid pharmacologic toxicity.

HIV is another needle-associated infection

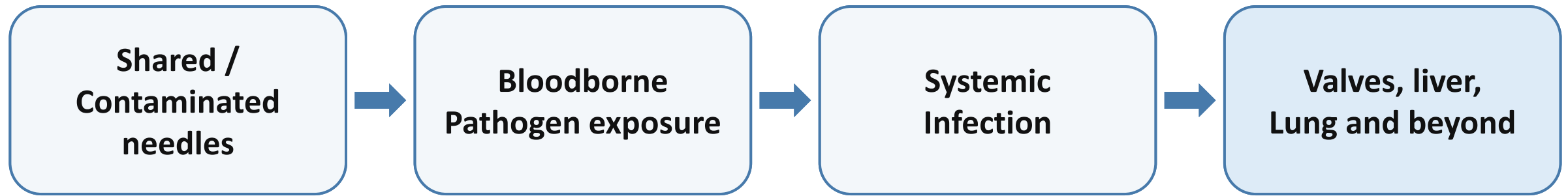
Shared injection equipment is linked to HIV transmission.

HIV infection has historically been a major complication in U.S. Injection-drug users.

This is an infection-related complication, not a direct opioid receptor effect.

Exposure through shared equipment is the relevant causal link.

A shared injection pathway reaches distant organs



Schematic

Different pathogens and anatomic pathways produce different lesions; The pathway is illustrative, not a universal sequence.

Acute injection-site pathology

Cutaneous lesion	Clinicopathologic significance
Abscess	Localized suppurative infection
Cellulitis	Inflammatory infection of skin / soft tissue
Ulceration	Breakdown at subcutaneous injection sites

Chronic cutaneous findings preserve exposure history

Repeated injection can leave scarring at puncture sites.

Hyperpigmentation may occur over commonly used veins.

Thrombosed veins are another described sequela.

Together these form a pattern of repetitive local injury.

Venous lesions differ from active infection

Active tissue lesions

Abscesses, cellulitis and ulceration

Require evaluation for infection and tissue damage

Chronic track lesions

Scarring, venous pigmentation, thrombosed veins

Indicate repeated local injury in the appropriate setting

Two renal patterns dominate the discussion

Amyloidosis

Associated generally with recurrent skin infections

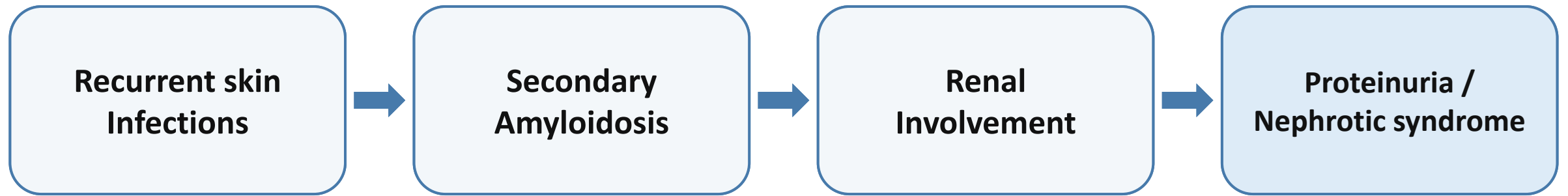
Can present with significant proteinuria

Focal and segmental glomerulosclerosis

Another recognized pattern in heroin-associated renal disease

Also causes proteinuria / nephrotic syndrome

Skin infection can be upstream of amyloidosis



Schematic

This is the causal association the textbook specifically makes for heroin-associated amyloid disease.

FSGS is a second glomerular injury pattern

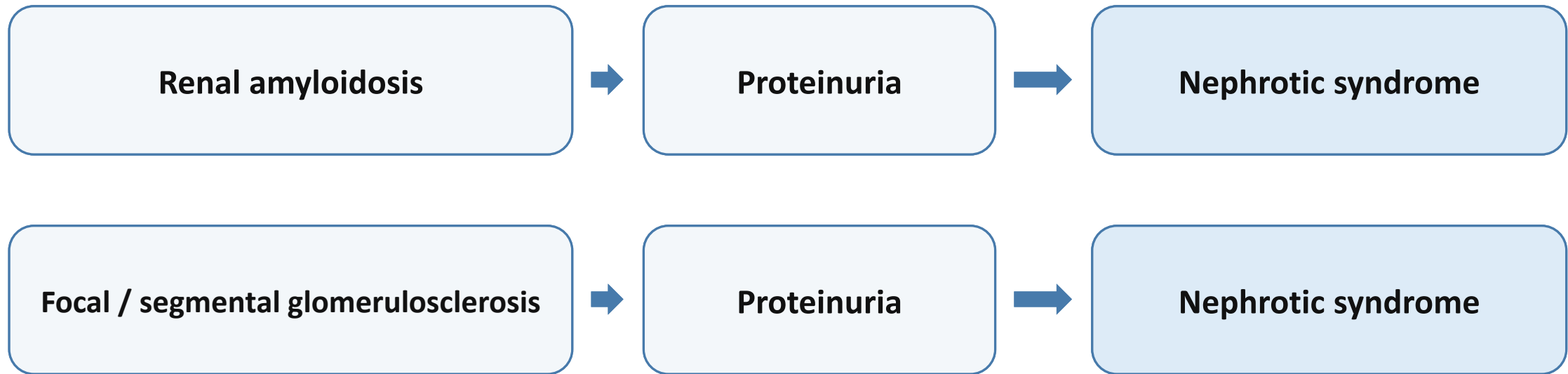
Focal and segmental glomerulosclerosis is a recognized renal lesion in heroin users.

The designation refers to sclerosis involving portions of some glomeruli.

The renal manifestation may include marked proteinuria.

FSGS must be distinguished from secondary amyloidosis despite a shared syndrome.

Different renal lesions converge on protein loss



Schematic: Independent renal pathways

Parallel injury pathways with a shared clinical phenotype; Amyloidosis does not cause FSGS in this figure.

Renal differential: Same syndrome, distinct lesions

Feature	Amyloidosis	FSGS
Textbook association	Often follows skin infections	Recognized separate heroin-associated lesion
Lesion category	Amyloid deposition	Focal segmental sclerosis
Potential phenotype	Proteinuria / nephrotic syndrome	Proteinuria / nephrotic syndrome
Relationship to skin infections	Generally secondary to recurrent infections	No such cause is specified here

Integrated organ map: One exposure, several paths

Brain / respiration

Direct opioid pharmacology

Lung

Edema, infection and foreign-body reaction

Heart / blood

Right-sided endocarditis; Arrhythmia

Skin / kidney

Injection injury; Infection-linked amyloid or FSGS

Exposure mechanism predicts type of pathology

Dominant exposure pathway	Expected category of injury
Opioid receptor agonism	CNS effects; respiratory suppression
Variable concentration / fentanyl	Unexpected overdose
Foreign particulate adulterants	Granulomatous reaction
Contaminated injection equipment	Skin infection, endocarditis, bloodborne viral infection
Chronic skin infection	Secondary renal amyloid disease

Case: Unexpected fentanyl exposure

CLINICAL STEM

Illustrative case — not patient data

A person without known opioid tolerance uses a drug believed to contain no fentanyl and becomes profoundly somnolent with severely suppressed breathing.

Which exposure uncertainty explains the rapid deterioration?

Unrecognized fentanyl content plus absent tolerance; The most immediate lethal mechanism is respiratory suppression.

Case: Injection use and pulmonary septic injury

CLINICAL STEM

Illustrative case — not patient data

A patient who injects heroin develops a valvular infection involving the right heart and then signs of pulmonary infection.

What valve-to-lung mechanism best links these findings?

Tricuspid/right-sided infective endocarditis with septic embolization to the lungs.

Case: Particulate-associated pulmonary lesion

CLINICAL STEM

Illustrative case — not patient data

Tissue from the lung contains foreign-body granulomas with particles highlighted by polarized light, sometimes within giant cells.

What exposure is suggested by this pattern?

Particulate cutting agents such as talc; This is a tissue reaction, not proof of an opioid concentration.

Case: Repeated skin infections and proteinuria

CLINICAL STEM

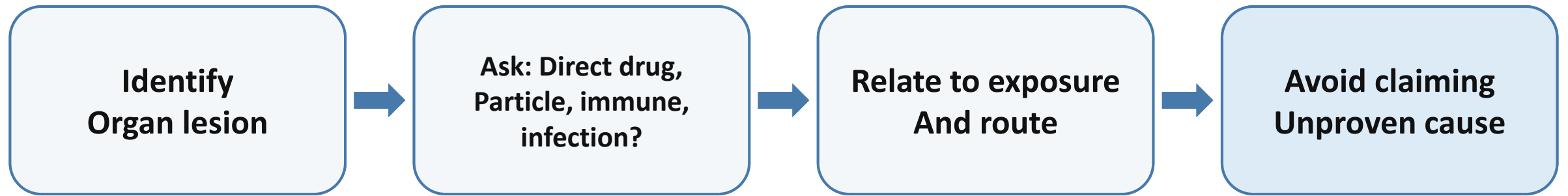
Illustrative case — not patient data

A person with longstanding subcutaneous injection-associated skin infections subsequently develops proteinuria and a nephrotic presentation.

Which renal lesion is specifically linked to the recurrent infection history?

Secondary amyloidosis. FSGS remains another heroin-associated renal pattern but is not stated to arise from those infections.

Clinicopathologic inference requires a causal category



Schematic

Opioid-related disease is not reducible to a single toxicologic mechanism.

Acute hazards to retain

Unexpected fentanyl exposure can be fatal in a person without tolerance.

Profound respiratory suppression is the usual acute mechanism of death.

Arrhythmia, cardiac arrest and severe pulmonary edema are other reported fatal mechanisms.

Timely naloxone can reverse opioid-mediated respiratory suppression.

Long-term pathology to retain

Injection-associated infections involve skin, right-sided valves, liver and lungs.

Particulate adulterants may produce pulmonary or systemic foreign-body granulomas.

Acute and chronic skin lesions reflect repeated injection-associated injury.

Renal amyloidosis and FSGS can each produce proteinuria and nephrotic syndrome.

Source and scope

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026). Chapter 9, “Opioids and Opiates,” pp. 387–388.

Parent section: “Injury by Nontherapeutic Agents (Drug Use Disorder),” p. 386, including Table 9.6.

Historical surveillance numbers are preserved as reported in the textbook. No independent epidemiologic update or original chapter-PDF verification was performed.

Figures in this lecture are original editable explanatory schematics; no diagnostic photographs are represented as authentic source images.