

Smoking and Other Diseases

Systemic pathology of tobacco smoke, passive exposure, and vaping

Cancer and chronic respiratory injury

Cardiovascular, reproductive, and systemic consequences

Second-hand smoke and EVALI

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Learning objectives

FOUNDATIONS

- Explain how tobacco exposure produces multisystem injury through distinct mechanisms.
- Associate smoking with major cancer sites, obstructive lung disease, and vascular events.
- Trace pregnancy, systemic, and passive-smoke consequences to the relevant exposure.
- Describe vaping-related pulmonary injury without equating vaping with harmlessness.

Smoking injury extends far beyond the lung

FOUNDATIONS

Malignancy

Multiple organs

Airways

COPD · asthma

Vessels

MI · stroke

Tobacco exposure

Pregnancy

Growth · preterm

Systemic

Diabetes · eye

Bystanders

Passive exposure

Schematic map of established associations; Not scaled by risk

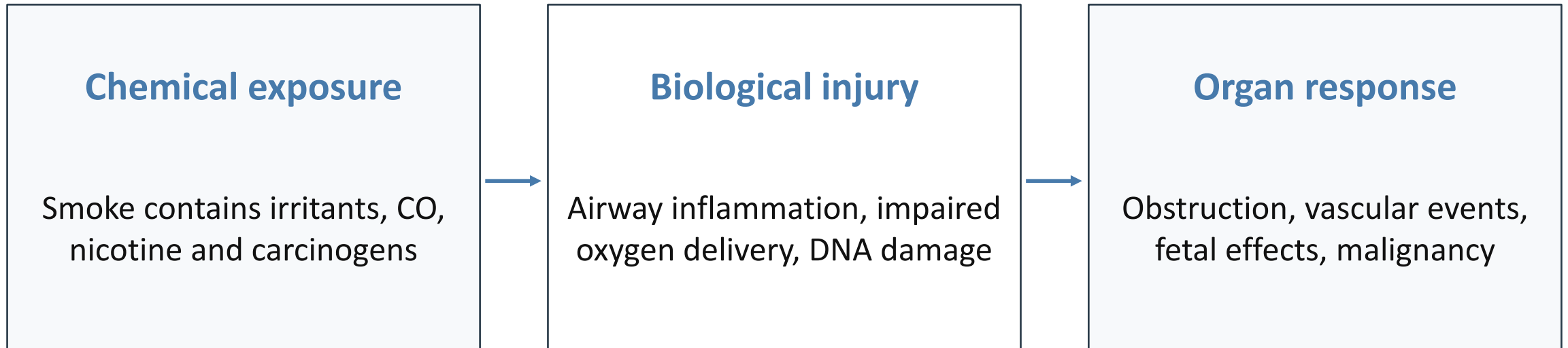
Exposure categories matter

FOUNDATIONS

- Active cigarette smoking: Direct inhalation of combustion products.
- Smokeless tobacco: Substantial oral carcinogenic risk, even without inhalation.
- Second-hand smoke: Involuntary exposure causing disease in nonsmokers.
- Vaping: Inhaled aerosol from an electronic device; Toxicological profile differs from cigarettes.

Multiple pathways connect exposure to disease

FOUNDATIONS



Mechanistic sequence — simplified conceptual schematic

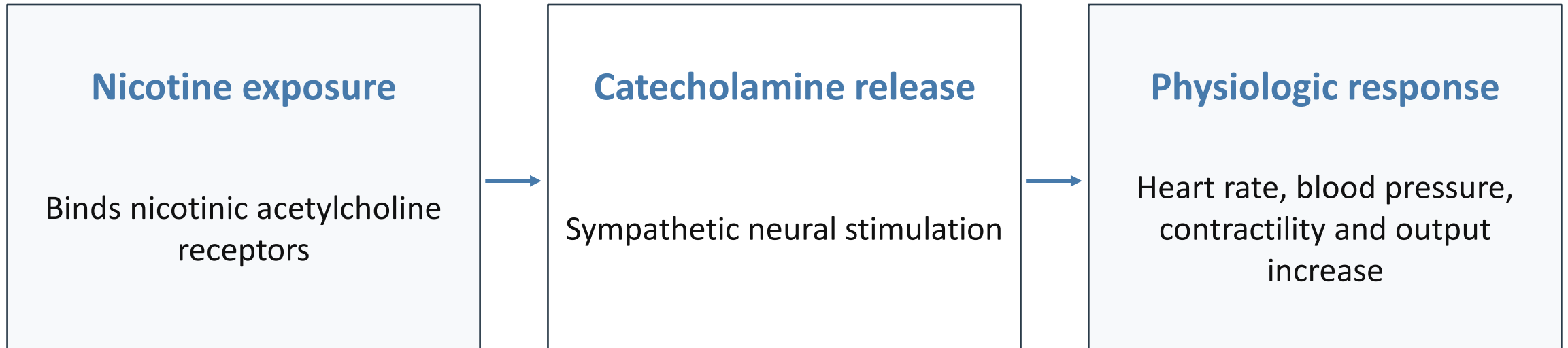
Tobacco smoke is a complex toxic mixture

FOUNDATIONS

- Approximately 7,000 chemicals in cigarette smoke.
- More than 60 components are identified as carcinogenic in the source.
- Examples include polycyclic aromatic hydrocarbons, nitrosamines, and aromatic amines.
- Individual compounds cause different patterns of epithelial, vascular, and systemic harm.

Nicotine produces rapid sympathetic effects

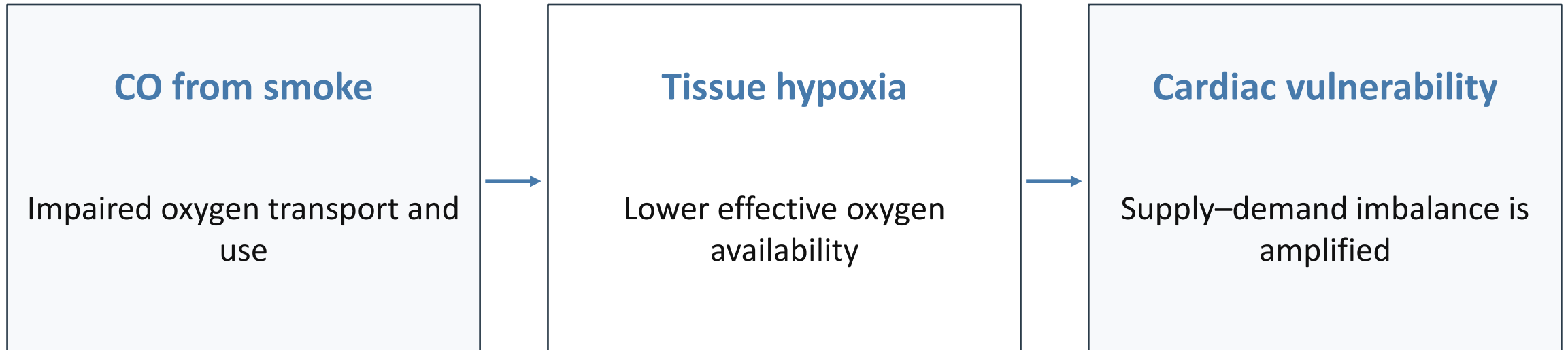
FOUNDATIONS



Mechanistic sequence — simplified conceptual schematic

Carbon monoxide reduces oxygen availability

FOUNDATIONS



Mechanistic sequence — simplified conceptual schematic

Smoking exposure accumulates over time

FOUNDATIONS

- Pack-years = packs smoked per day $\times$ years of smoking.
- Exposure intensity and duration both matter for cumulative harm.
- Pack-years describe smoking history; They do not capture all individual susceptibility.
- Risk varies by disease and is modified by competing exposures.

Smoking cessation changes long-term risk

FOUNDATIONS

- A marked decline in cardiac mortality risk within five years of cessation.
- Lung cancer mortality also declines after quitting, but excess risk persists for decades.
- Stopping before pregnancy is associated with normalization of infant birth weight in the source.
- Cessation reduces future exposure; It does not erase established pathology immediately.

Smoking-associated malignancies span many organs

CANCER

Aerodigestive

Oral · larynx · esophagus

Thorax

Lung / bronchus

Abdominal

Pancreas · liver · stomach

Tobacco carcinogenesis

Urinary

Kidney · ureter · bladder

Other epithelial

Colon · cervix

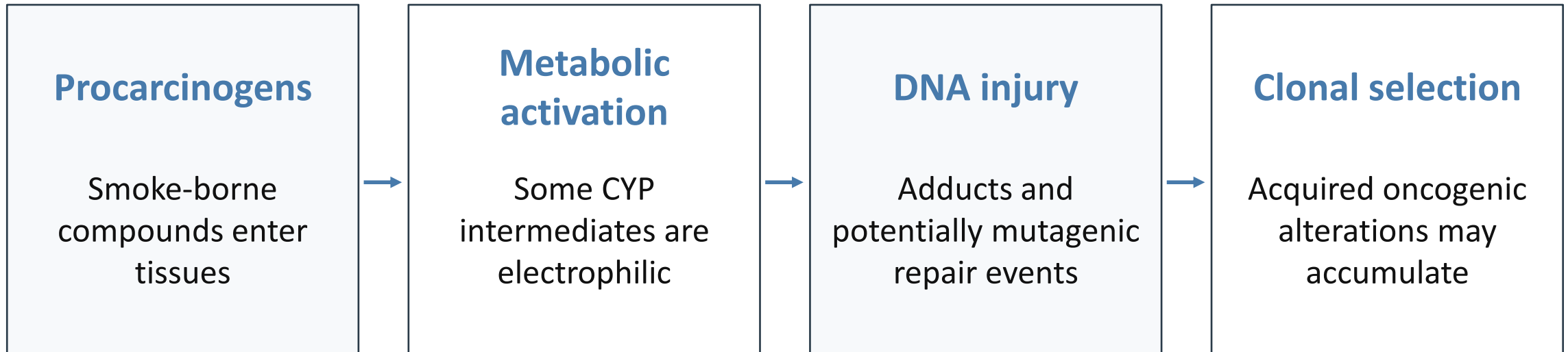
Hematologic

Acute myeloid leukemia

Schematic map of established associations; Not scaled by risk

Chemical carcinogenesis: Core sequence

CANCER



Mechanistic sequence — simplified conceptual schematic

Carcinogen–organ relationships are site-specific

CANCER

- Table 9.4 lists suspected organ-specific carcinogens rather than definitive single-cause assignments.
- Nitrosamines and polycyclic aromatic hydrocarbons recur across exposed sites.
- The bladder is linked to aromatic amines, including 4-aminobiphenyl and 2-naphthylamine.
- Causal smoking–cancer associations are broader than any one chemical mapping.

Selected suspected organ-specific carcinogens

CANCER

Site	Compounds identified
Lung / larynx	PAHs; NNK; Polonium-210
Esophagus	NNN
Pancreas	NNK
Bladder	4-Aminobiphenyl; 2-naphthylamine

Upper aerodigestive cancers share exposure routes

CANCER

- The source links tobacco with cancers of the oropharynx, larynx, and esophagus.
- Local mucosal contact is relevant for smoked and smokeless tobacco.
- The co-exposure to alcohol strengthens the association with oral and laryngeal cancer.
- Do not infer equal risk magnitudes for all sites from a common exposure.

Smokeless tobacco also produces cancer risk

CANCER

- Snuff and chewing tobacco are harmful even without inhaled smoke.
- Oral carcinogenesis is a major smoking-independent tobacco consequence.
- NNK, NNN, and polonium-210 among suspected agents for oral cavity snuff exposure.
- Absence of combustion does not imply absence of carcinogens.

Esophageal and pancreatic cancer associations

CANCER

- Esophageal and pancreatic cancers appear's smoking-related cancer list.
- Table 9.4 associates esophageal carcinogenesis with NNN.
- The same table lists NNK as a suspected carcinogen associated with pancreatic cancer.
- These listings do not establish histologic subtype or molecular specificity.

Bladder carcinogenesis illustrates systemic delivery

CANCER

- Bladder cancer is an established smoking-associated malignancy in the source.
- Table 9.4 names 4-aminobiphenyl and 2-naphthylamine as suspected agents.
- The organ-specific listing distinguishes this risk from direct airway irritation.
- Exposure history remains clinically relevant for urothelial malignancy.

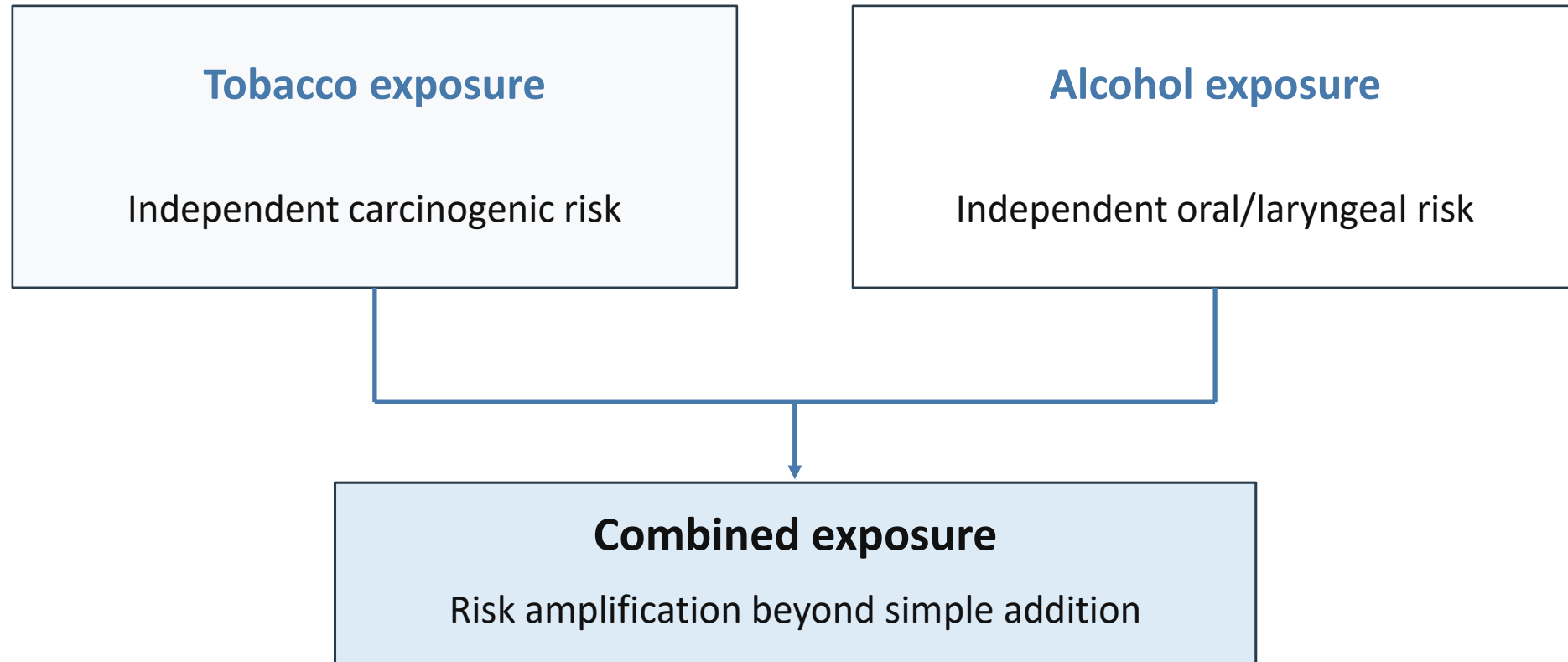
Other epithelial and hematologic malignancies

CANCER

- The textual list includes kidney, cervical, liver, and colon cancers.
- Figure 9.10 additionally depicts stomach and upper urinary tract cancers.
- Hematopoietic disease includes acute myeloid leukemia in the source illustration.
- An organ association does not justify an invented mutation panel or tumor-grade pattern.

Smoking and alcohol can interact multiplicatively

CANCER



Convergent contributors — not a temporal sequence

Co-exposures complicate cancer attribution

CANCER

- Smoking increases the risk of lung cancer associated with asbestos and uranium exposure.
- The source describes a roughly tenfold higher lung carcinoma incidence in exposed workers who smoke versus those who do not.
- A combined exposure history is needed in occupational clinical assessment.
- This example comes from the adjacent lung-cancer discussion.

Applied example: Hematuria in a smoker

CANCER

Clinical observation

An adult with a long smoking history presents with painless hematuria. A bladder lesion is detected during clinical evaluation.

Pathology interpretation

Smoking is a relevant carcinogenic exposure; Aromatic amines are among suspected bladder-specific tobacco carcinogens. Morphology and clinical workup—not exposure alone—establish diagnosis.

Pulmonary effects arise from several mechanisms

RESPIRATORY

Small airways

Persistent obstruction

Alveoli

Emphysematous injury

Bronchi

Mucus / bronchitis

Inhaled smoke

Asthma

Exacerbation

Infections

TB and pneumonia

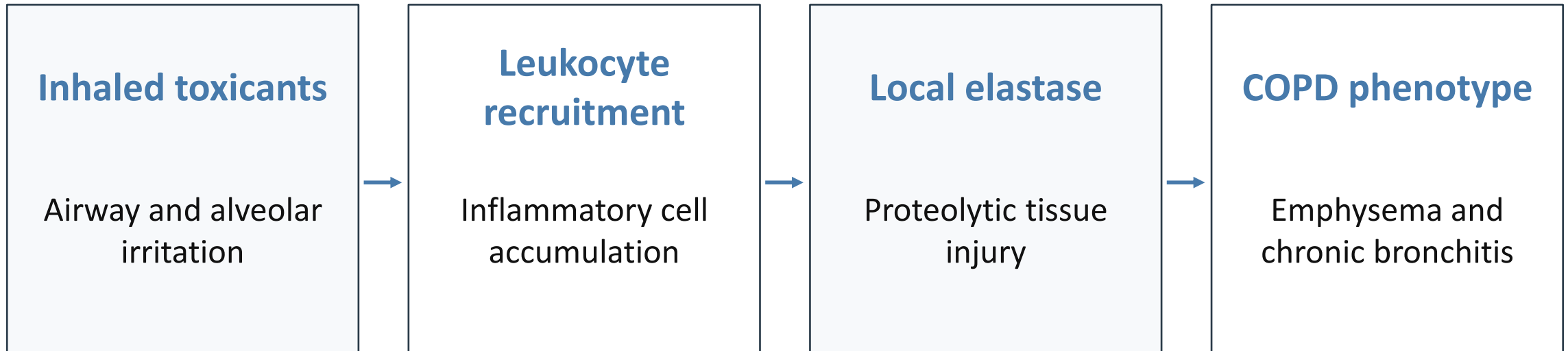
Cilia

Irritant injury

Schematic map of established associations; Not scaled by risk

Smoking recruits inflammatory cells into the lung

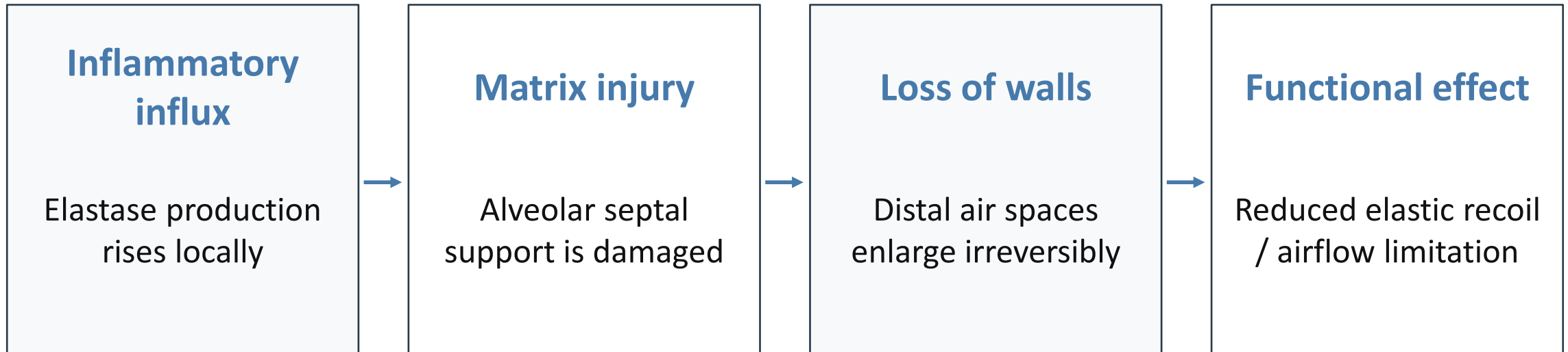
RESPIRATORY



Mechanistic sequence — simplified conceptual schematic

Protease-mediated injury contributes to emphysema

RESPIRATORY



Mechanistic sequence — simplified conceptual schematic

Emphysema is an anatomic diagnosis

RESPIRATORY

- Emphysema by irreversible enlargement of distal air spaces.
- Destruction of alveolar walls accompanies the enlarged spaces.
- Smoking-related COPD commonly shows centriacinar emphysema.
- Emphysema and chronic bronchitis frequently coexist.

Centriacinar versus panacinar patterns

RESPIRATORY

Centriacinar

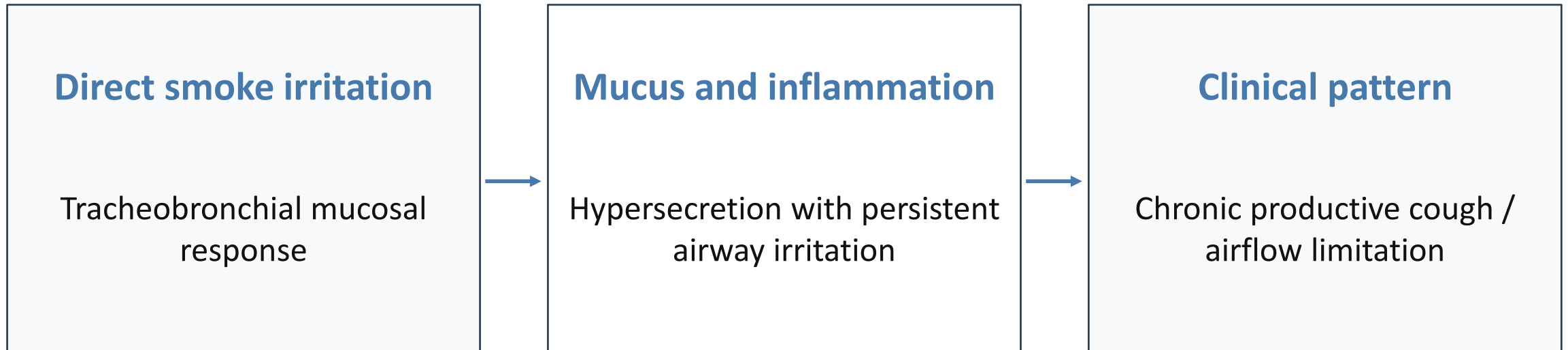
- Proximal acinus is preferentially affected.
- Predominates in heavy smoking-related COPD.
- Typically more pronounced in upper lobes.

Panacinar

- Uniform acinar enlargement.
- Associated with α_1 -antitrypsin deficiency.
- Smoking can exacerbate this phenotype.

Chronic bronchitis: The mucus pathway

RESPIRATORY



Mechanistic sequence — simplified conceptual schematic

Emphysema and chronic bronchitis coexist

RESPIRATORY

Emphysema

- Primary structural locus: Distal air spaces.
- Core process: Alveolar wall destruction.
- Dominant function: Impaired elastic recoil.

Chronic bronchitis

- Primary structural locus: Conducting airways.
- Core process: Airway inflammation and mucus.
- Dominant symptom: Productive cough.

Cigarette smoke damages the mucociliary barrier

RESPIRATORY

- Formaldehyde and nitrogen oxides are identified as toxic to cilia.
- Ciliary injury undermines normal mechanical airway protection.
- Mucosal irritation promotes increased mucus production.
- These effects complement leukocyte-mediated injury in COPD.

Smoking exacerbates asthma

RESPIRATORY

- The main topic explicitly identifies asthma exacerbation as a tobacco effect.
- Smoke acts as an airway irritant and can trigger bronchospastic symptoms.
- Asthma is generally associated with variable airflow obstruction.
- Coexisting fixed obstruction can complicate asthma–COPD distinction.

Tuberculosis and respiratory infection risks

RESPIRATORY

- Smoking increases the risk of pulmonary tuberculosis.
- Figure 9.10 also lists pneumonia and other respiratory effects.
- Airway epithelial/ciliary damage provides a plausible impaired-defense context.
- The supplied subsection provides associations, not infection-specific risk estimates.

Clinical distinction: Obstruction patterns

RESPIRATORY

COPD-associated injury

- Smoking exposure is a major etiologic factor.
- Airway and/or alveolar pathology causes persistent limitation.
- Emphysema and chronic bronchitis are frequent manifestations.

Asthma exacerbation

- Smoke may act as an acute irritant trigger.
- Symptoms often vary with bronchospasm.
- A reversible component may overlap with COPD.

Applied example: Progressive dyspnea

RESPIRATORY

Clinical observation

An older smoker develops persistent exertional breathlessness and a chronic productive cough.

Pathology interpretation

Chronic bronchitis and emphysema can coexist in smoking-related COPD. Mechanisms include mucus hypersecretion, leukocyte recruitment, and proteolytic alveolar injury.

Smoking increases atherosclerotic and cardiac risk

CARDIOVASCULAR

Platelets

Aggregation

Oxygen supply

CO · lung disease

Cardiac demand

Adrenergic effects

Vascular / cardiac injury

Electrical stability

Lower VF threshold

Atherosclerosis

MI / stroke

Co-risk factors

HTN · cholesterol

Schematic map of established associations; Not scaled by risk

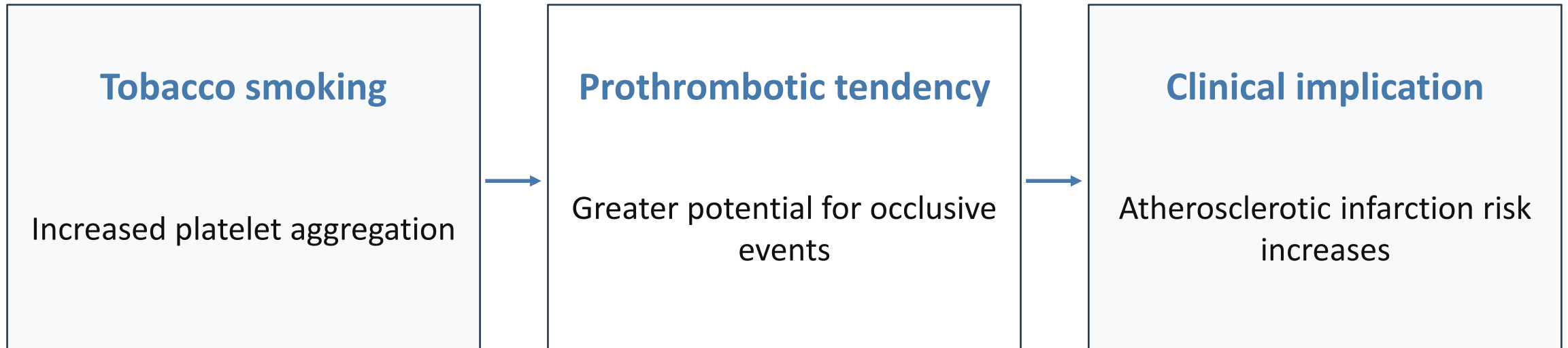
Atherosclerosis underlies major outcomes

CARDIOVASCULAR

- The source links smoking to atherosclerosis and its clinical complications.
- Myocardial infarction and stroke are explicitly identified.
- Figure 9.10 also includes aortic aneurysm and coronary artery disease.
- Multiple biological mechanisms plausibly act together.

Platelet effects support acute vascular events

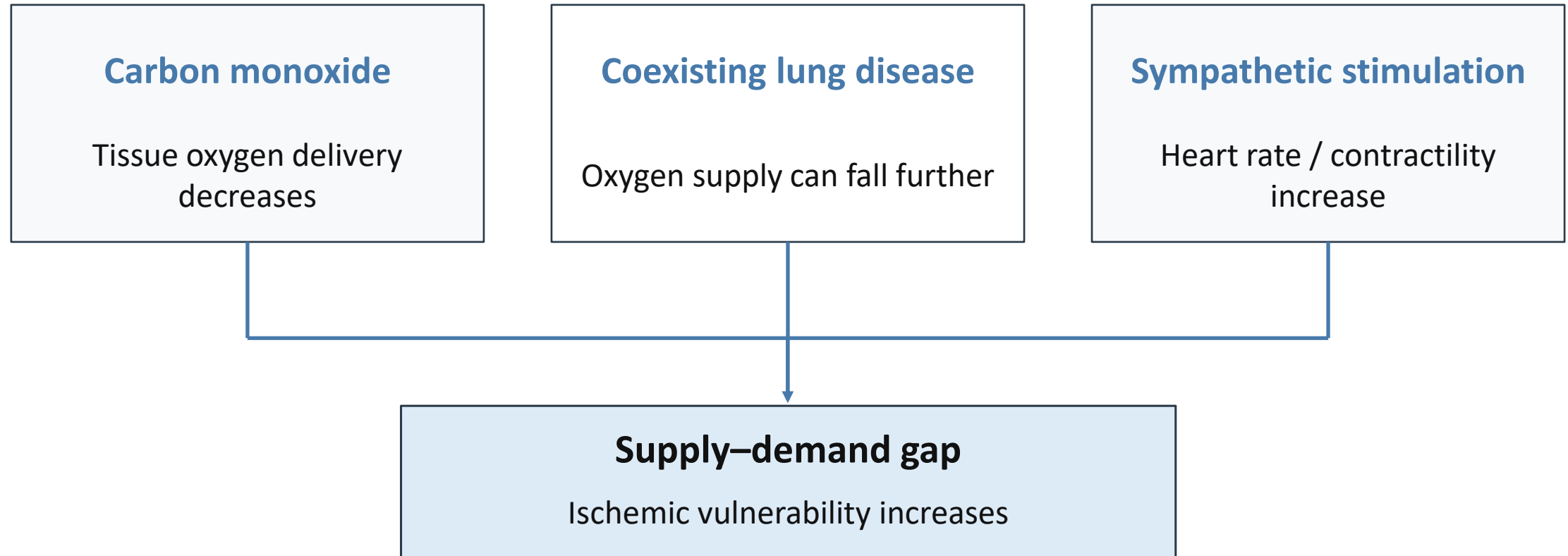
CARDIOVASCULAR



Mechanistic sequence — simplified conceptual schematic

Smoking worsens myocardial oxygen balance

CARDIOVASCULAR



Convergent contributors — not a temporal sequence

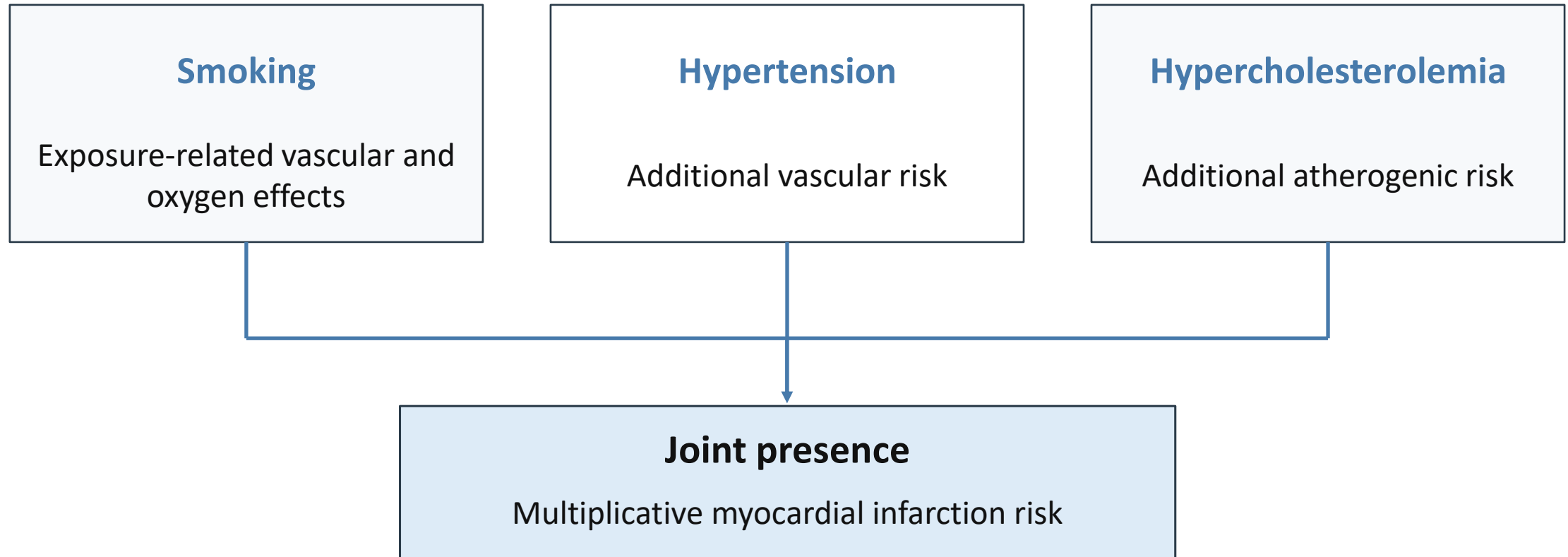
Cardiac electrophysiology is also affected

CARDIOVASCULAR

- A decreased threshold for ventricular fibrillation.
- Increased myocardial demand and reduced oxygen supply occur simultaneously.
- Smoking-related cardiovascular risk cannot be reduced to plaque burden alone.
- This is a pathophysiologic link, not a patient-specific arrhythmia prediction.

Smoking amplifies traditional cardiac risk factors

CARDIOVASCULAR



Convergent contributors — not a temporal sequence

Stroke and aortic disease broaden vascular scope

CARDIOVASCULAR

- Stroke is named as a major atherosclerotic complication of tobacco use.
- The source illustration lists aortic aneurysm and atherosclerosis.
- Vascular injury therefore spans cerebral, coronary, and large-vessel territories.
- Smoking history matters even when pulmonary symptoms are absent.

Applied example: Acute coronary syndrome

CARDIOVASCULAR

Clinical observation

A smoker with hypertension and hypercholesterolemia presents with acute chest pain and ischemic ECG changes.

Pathology interpretation

The combination of smoking with hypertension and hypercholesterolemia is described as multiplicative for MI risk; CO-related oxygen impairment and platelet aggregation provide complementary mechanisms.

Pregnancy and reproductive outcomes

REPRODUCTION

Gestation

Preterm birth

Pregnancy loss

Spontaneous abortion

Placental–fetal

Growth restriction

Maternal tobacco exposure

Fetal brain

Nicotine injury

Pregnancy site

Ectopic pregnancy

Fertility

Reduced in women

Schematic map of established associations; Not scaled by risk

Maternal smoking harms pregnancy outcome

REPRODUCTION

- Spontaneous abortion and preterm delivery are explicitly linked to maternal smoking.
- Intrauterine growth restriction is another central adverse outcome.
- The source also identifies ectopic pregnancy in its multisystem risk list.
- These are distinct outcomes; None should be equated with the others.

Fetal growth is sensitive to exposure timing

REPRODUCTION

Smoking during pregnancy

- Maternal tobacco exposure can restrict fetal growth.
- Intrauterine growth retardation is linked to lower birth weight.

Stopped before pregnancy

- Normal infant birth weights in this group.
- The finding supports cessation before conception, not a guaranteed individual outcome.

Nicotine is relevant to fetal development

REPRODUCTION

- Nicotine crosses beyond the addiction question into developmental toxicity.
- The preceding tobacco overview associates nicotine exposure with impaired fetal brain development.
- Preterm birth and stillbirth are also identified as nicotine-related concerns.
- This does not isolate nicotine as the only harmful constituent of cigarette smoke.

Additional reproductive and developmental effects

REPRODUCTION

- Figure 9.10 includes reduced female fertility and ectopic pregnancy.
- Orofacial clefts are listed as associated with maternal smoking.
- Male erectile dysfunction is included among tobacco-related outcomes.
- Clinical mechanisms are not specified for every listed disease in this subsection.

Applied example: Antenatal exposure

REPRODUCTION

Clinical observation

A patient planning pregnancy asks whether cessation matters if she has smoked for years.

Pathology interpretation

Maternal smoking with loss, preterm delivery, and intrauterine growth restriction; Stopping before pregnancy is associated with normal birth weight in the cited text.

Other smoking-linked chronic diseases

OTHER SYSTEMS

Metabolic

Type 2 diabetes

Immune

Rheumatoid arthritis

Ophthalmic

Macular degeneration

Systemic associations

Ocular

Cataract / blindness

Oral

Periodontitis

Skeletal

Hip fractures

Schematic map of established associations; Not scaled by risk

Type 2 diabetes belongs in the tobacco burden

OTHER SYSTEMS

- The source explicitly names type 2 diabetes as smoking-associated.
- Figure 9.10 repeats diabetes among chronic diseases linked to smoking.
- The topic does not provide a site-specific causal molecular sequence.
- Avoid inventing a numerical diabetes risk or biomarker threshold.

Rheumatoid arthritis and immune effects

OTHER SYSTEMS

- Rheumatoid arthritis appears in the source list of smoking-related diseases.
- Figure 9.10 includes decreased immune function.
- These associations complement respiratory infection vulnerability.
- The supplied unit does not specify serologic or histologic subtypes.

Ophthalmic consequences are not limited to cataracts

OTHER SYSTEMS

- Age-related macular degeneration is named in the text.
- The associated disease figure lists cataracts and blindness.
- Vision-threatening injury is part of the systemic smoking phenotype.
- The source does not stratify by clinical stage or ophthalmic imaging criteria.

Periodontal disease and skeletal injury

OTHER SYSTEMS

- Periodontitis is included in the Surgeon General-derived disease map.
- Hip fractures are also listed among chronic smoking consequences.
- The figure additionally includes overall diminished health.
- These endpoints often receive less attention than COPD and cancer.

Applied example: Multimorbidity

OTHER SYSTEMS

Clinical observation

A long-term smoker has COPD, coronary disease, diabetes, and visual impairment.

Pathology interpretation

These diagnoses span several established smoking-linked systems. The exposure is clinically relevant across organs; Individual disease attribution still requires appropriate clinical assessment.

Second-hand smoke creates involuntary exposure

PASSIVE SMOKE

Adults

Coronary events

Nonsmokers

Lung cancer

Children

Asthma / infections

**Environmental tobacco
smoke**

Homes

Ongoing exposure

Measurement

Blood cotinine

Policy

Exposure reduction

Schematic map of established associations; Not scaled by risk

Passive smoke is not biologically inert

PASSIVE SMOKE

- The subsection states that environmental tobacco smoke carries many active-smoking risks.
- Nonsmokers may acquire smoking-associated lung cancer risk.
- Coronary atherosclerosis and fatal myocardial infarction are also highlighted.
- Household exposure is particularly concerning for children.

Passive exposure increases lung cancer risk

PASSIVE SMOKE

- Relative risk near 1.3 for exposed versus unexposed nonsmokers.
- This is a relative comparison, not a 30% absolute probability of cancer.
- The source reports historical U.S. Mortality attributable to second-hand smoke.
- Present-day incidence or mortality must not be inferred from the textbook estimate.

Passive smoke also contributes to cardiac deaths

PASSIVE SMOKE

- Coronary atherosclerosis and fatal infarction after passive exposure.
- It cites historical U.S. Estimates of 30,000–60,000 associated cardiac deaths annually.
- These are source-era estimates, not newly updated counts.
- Environmental exposure should be documented in nonsmokers with vascular disease.

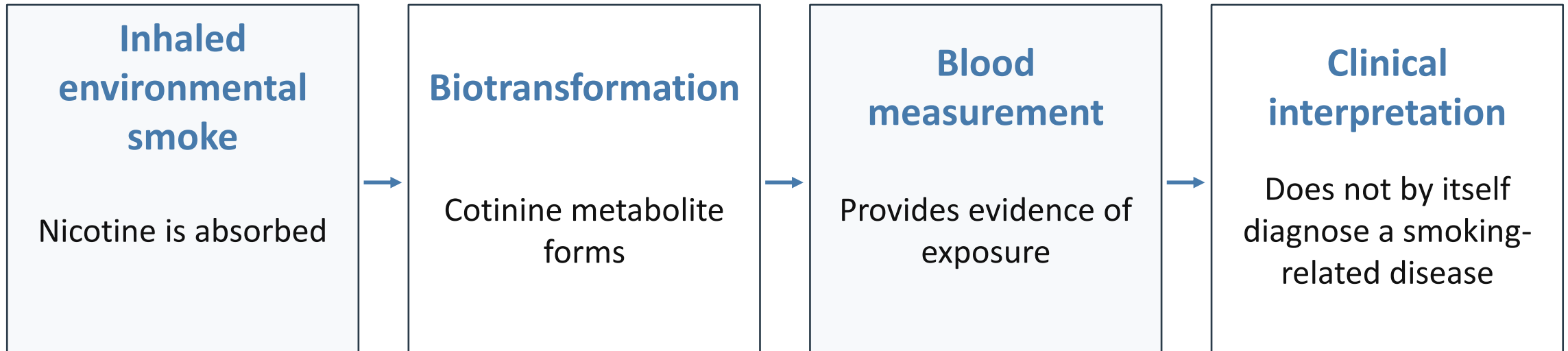
Children are susceptible to household smoke

PASSIVE SMOKE

- Children living with smokers have increased respiratory illness frequency.
- Asthma is specifically identified among those illnesses.
- The household remains a major source of involuntary exposure.
- Risk assessment must include cohabitants, not only the patient's own smoking.

Cotinine is an exposure marker, not a diagnosis

PASSIVE SMOKE



Mechanistic sequence — simplified conceptual schematic

Tobacco control reduces passive exposure

PASSIVE SMOKE

- The source reports a greater than 70% reduction in median U.S. Nonsmoker cotinine levels since around 2000.
- It attributes the fall substantially to public nonsmoking policies.
- Lower population cotinine does not eliminate household exposure.
- Population indicators and individual household risks should be distinguished.

Applied example: Child with asthma

PASSIVE SMOKE

Clinical observation

A child with recurrent wheeze lives with an adult who smokes indoors. The child does not use tobacco.

Pathology interpretation

Environmental tobacco smoke is a clinically relevant exposure. More frequent asthma and respiratory illness in children living with smokers.

Vaping has a distinct but consequential risk profile

VAPING



Schematic map of established associations; Not scaled by risk

Cigarette smoking versus vaping

VAPING

Combustible cigarettes

- Inhaled combustion-related toxicants.
- Established multisystem chronic disease burden.
- CO and numerous identified carcinogens.

Vaping devices

- Aerosolized nicotine and other chemicals.
- Potentially reduced exposure to some combustion toxins.
- Addiction and lung injury remain possible.

Vaping is not equivalent to harmlessness

VAPING

- Aerosolized nicotine and flavoring delivery.
- Vaping is used by some long-term smokers and recreational users.
- The subsection flags use among adolescents and children.
- Reported harms include nicotine addiction, respiratory symptoms, and chemical lung injury.

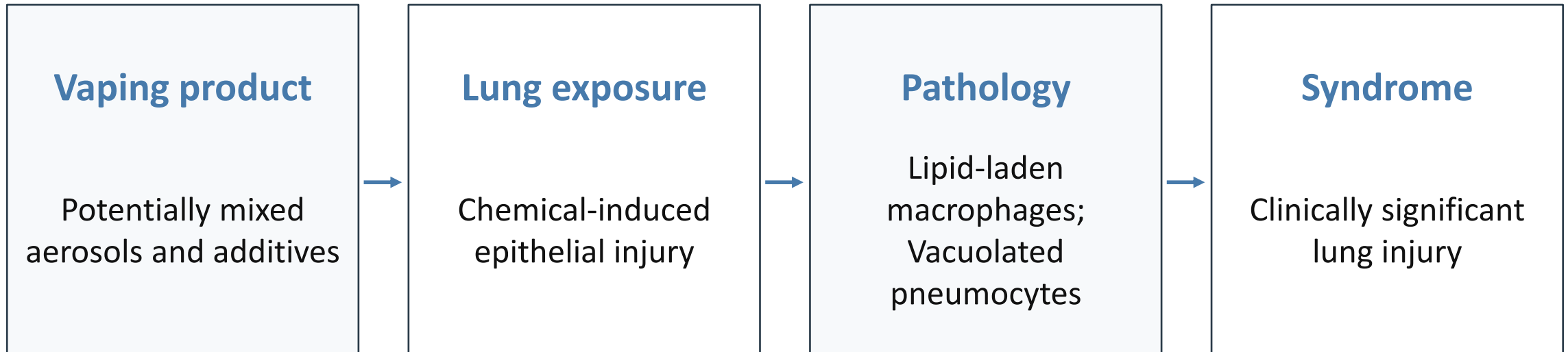
EVALI emerged as a severe acute lung injury

VAPING

- EVALI means e-cigarette or vaping product use–associated lung injury.
- The source dates recognition of the syndrome to 2019.
- Thousands of cases and dozens of deaths were reported during the outbreak.
- Its pathologic features suggest chemical-induced pneumonitis.

EVALI: Exposure and tissue response

VAPING



Mechanistic sequence — simplified conceptual schematic

EVALI morphology is suggestive, not specific

VAPING

- The source describes lipid-laden alveolar macrophages.
- Vacuolated pneumocytes are another reported microscopic finding.
- Together they suggest a chemically mediated pneumonitis.
- These findings alone do not identify one unique causative substance.

Vitamin E acetate: Preserve causal uncertainty

VAPING

- Many affected patients reported mixtures including cannabinoids and nicotine.
- Vitamin E acetate is described as suspected of causing lung damage.
- The source does not establish a uniform exposure composition across cases.
- Do not misstate association with vitamin E acetate as proven causation for every EVALI case.

Applied example: Vaping and pneumonitis

VAPING

Clinical observation

A young adult with recent vaping develops severe respiratory symptoms. Lung tissue is reported to contain vacuolated pneumocytes and lipid-laden alveolar macrophages.

Pathology interpretation

Vaping-associated lung injury enters the clinical differential. The microscopy is supportive of chemical injury but is not by itself pathognomonic of EVALI.

Exposure routes and consequences

SYNTHESIS

Exposure	Illustrative harms
Active smoking	COPD, cancers, myocardial infarction, stroke, fetal effects
Smokeless tobacco	Oral carcinogenesis
Passive smoke	Lung cancer, coronary events, childhood asthma
Vaped aerosols	Nicotine dependence, respiratory symptoms, EVALI

Mechanism-to-disease synthesis

SYNTHESIS

- Carcinogenic compounds → DNA injury → malignancies in multiple organs.
- Irritants and leukocyte elastase → airway and alveolar injury → COPD.
- Platelet aggregation and oxygen imbalance → atherosclerotic events and arrhythmia susceptibility.
- Maternal and passive exposure → fetal and bystander harms, even without direct smoking.

Clinical synthesis: Exposure history is pathology history

SYNTHESIS

- Document active exposure intensity, duration, cessation, and other tobacco products.
- Ask about second-hand smoke when patients do not smoke themselves.
- Distinguish vaping products and mixtures from combustible tobacco.
- Assess systemic manifestations rather than restricting review to the lungs.

Selected references

SYNTHESIS

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