

Neisserial Infections

Meningococcus · Gonococcus · Mucosal invasion · Immune evasion

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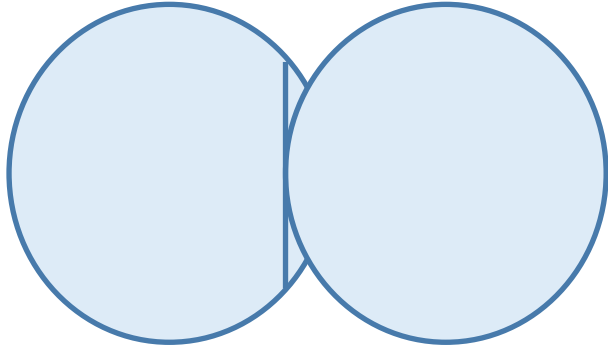
Learning objectives

- Distinguish the portals of entry and major diseases caused by the two pathogenic *Neisseria* species.
- Connect epithelial invasion, complement evasion and antigenic variation with clinical outcomes.
- Recognize the morphologic basis of pyogenic meningitis and gonococcal pelvic inflammation.
- Interpret dissemination, neonatal disease and important diagnostic pitfalls.

Two organisms, contrasting clinical syndromes

Dimension	N. Meningitidis	N. Gonorrhoeae
Usual entry	Oropharynx	Genital, pharyngeal or anorectal mucosa
Major disease	Meningitis; Septicemia	Urethritis; Cervicitis; PID
Dissemination	Blood to meninges and other sites	Septic arthritis with skin lesions
Shared vulnerability	Terminal complement deficiency	Terminal complement deficiency

Gram-negative diplococci: The shared morphology



Adjoining flattened faces

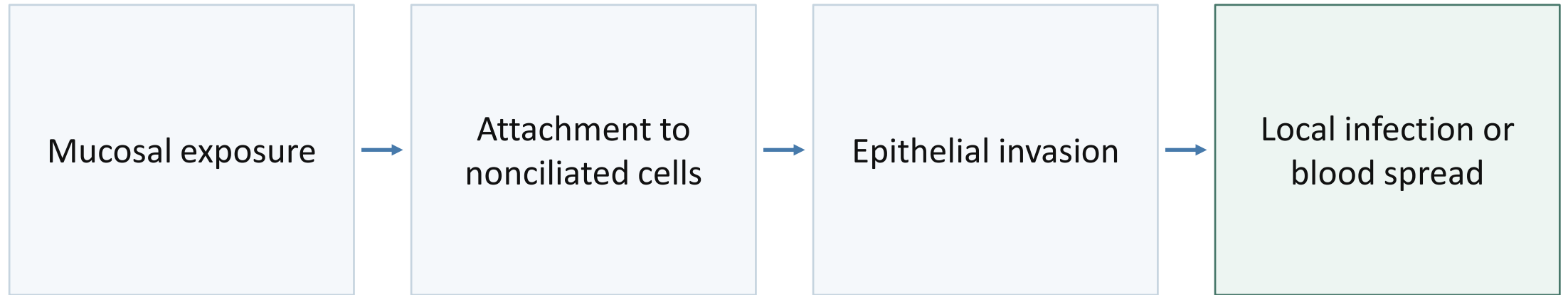
Original diagram · not a Gram stain

- Paired cocci are flattened along their adjoining surfaces.
- The resulting profile resembles paired coffee beans.
- Morphology alone does not determine which *Neisseria* species is present.

Nutritional requirements shape laboratory recovery

- The pathogenic *Neisseria* species described here are aerobic and fastidious.
- They grow best on enriched media, including chocolate agar.
- Culture remains important in appropriate settings; The clinical specimen and diagnostic question determine test selection.

Anatomic site determines the initial disease



Pathogenic *Neisseria* first engage exposed mucosal epithelium.

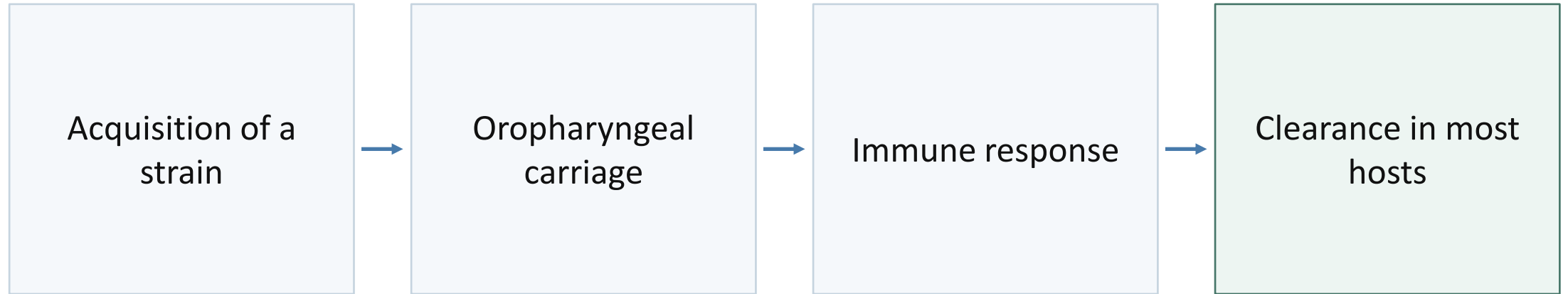
Transmission and colonization are not synonymous with disease

Concept	Meningococcus	Gonococcus
Acquisition	Respiratory exposure	Sexual or perinatal exposure
Typical first site	Oropharynx	Genital or other exposed mucosa
Early outcome	Colonization may be cleared	Local mucosal inflammation may follow
Severe outcome	Meningitis / sepsis	Upper tract disease / dissemination

Meningococcal carriage begins in the oropharynx

- *N. Meningitidis* commonly colonizes the oropharyngeal mucosa.
- Respiratory spread introduces the organism to new hosts.
- Most colonized individuals mount an immune response and eliminate the organism.

Carriage and protective immunity



The resulting immunity is protective against later exposure to the same serotype.

Why close-contact settings matter

- Crowded quarters create opportunities for respiratory transmission.
- College dormitories and military barracks are textbook examples.
- The pathologic risk is not crowding alone: Exposure to a strain lacking preexisting immunity matters.

A new strain may bypass prior serotype immunity

- The capsule defines several meningococcal serogroups.
- Prior immunity to one serotype need not protect against all other strains.
- The source attributes many invasive cases to encountering a new, unfamiliar strain.

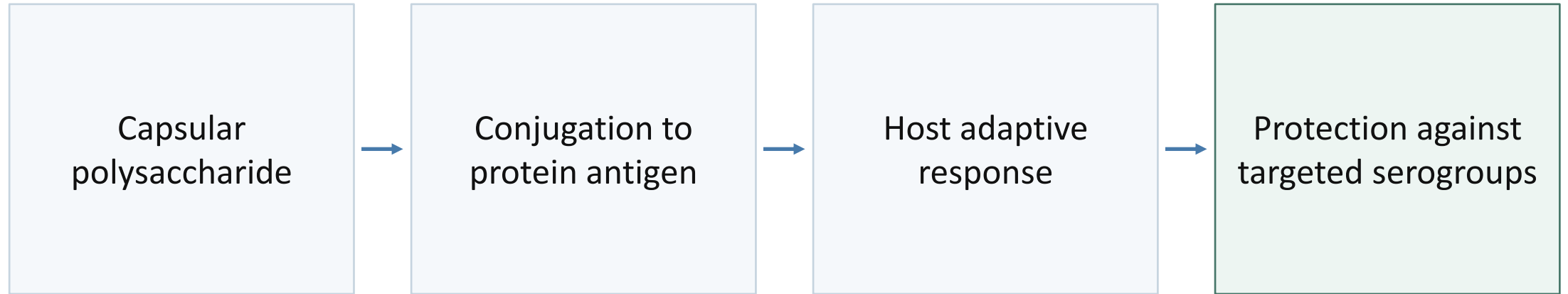
Population susceptibility: Exposure and host defense

Setting	Relevant mechanism	Implication
Children	Immune experience may be limited	Susceptibility to new strains
Adolescents / young adults	Close-quarter contact	Clusters may occur
Older adults	Recognized affected age group	Bacterial meningitis remains relevant
Complement deficiency	Impaired terminal complement killing	Disproportionately high invasive risk

Meningococcal serogroups have vaccine implications

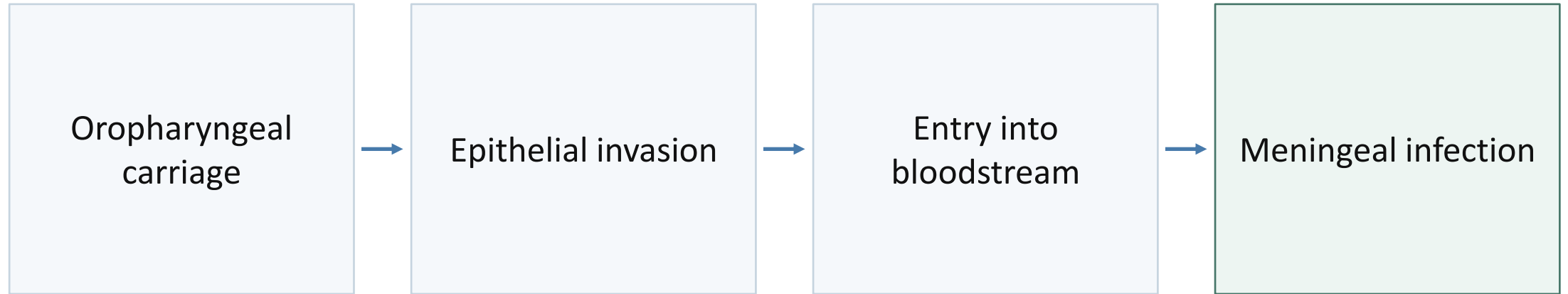
- Multiple meningococcal capsular serogroups exist.
- Conjugate capsular polysaccharide vaccines targeting A, C, W and Y.
- A separate recombinant protein vaccine strategy targets serogroup B.
- The target antigen and vaccine platform therefore differ across serogroups.

Conjugate vaccine: Antigen delivery principle



A polysaccharide–protein conjugate is not the same platform as a serogroup B protein vaccine.

The meningococcal invasive-disease sequence

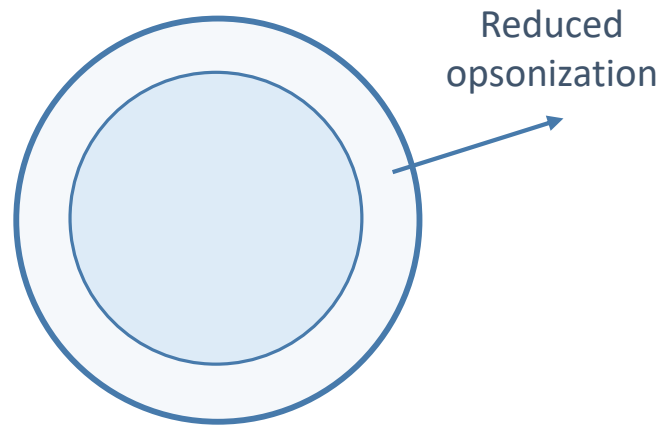


Invasive progression is exceptional relative to colonization.

Epithelial breach is the critical transition

- Carriage is confined to an exposed mucosal surface until the organism invades.
- To cause meningitis, *N. Meningitidis* must cross respiratory epithelium and reach the blood.
- Invasion is necessary but not sufficient: Circulating bacteria must evade host defenses.

The meningococcal capsule promotes bloodstream survival

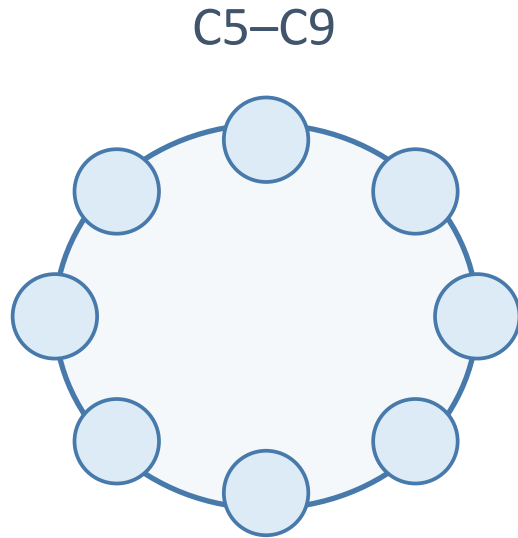


Outer capsule

Schematic bacterial envelope

- Capsular material impedes opsonization by complement components.
- Reduced opsonization limits efficient clearance of circulating organisms.
- The bloodstream is the central dissemination compartment before meningeal infection.

Terminal complement assembles the membrane attack complex



Terminal complement pore (conceptual)

Schematic, not molecular scale

- The terminal pathway involves C5 through C9.
- Assembly of the membrane attack complex damages susceptible bacterial membranes.
- This defense is particularly consequential in *Neisseria* infection.

Loss of C5–C9 produces exceptional susceptibility

A 1,000- to 2,000-fold increase in serious meningococcal infection among people with inherited terminal complement defects.

The numerical estimate is cited as a textbook statement; It is not a contemporary population risk estimate.

Complement blockade creates an acquired risk state

- Robbins also identifies patients receiving inhibitors of membrane attack complex formation.
- Examples mentioned include complement-directed treatment for paroxysmal nocturnal hemoglobinuria and hemolytic uremic syndrome.
- The mechanism parallels inherited terminal complement deficiency: Impaired membrane attack complex function.

Three checkpoints in meningococcal pathogenesis

Checkpoint	Host defense	Bacterial advantage
Oropharynx	Mucosal immune response	Successful colonization
Bloodstream	Complement opsonization / killing	Capsule-associated survival
Meninges	Inflammatory host response	Pyogenic meningeal disease

Acute pyogenic meningitis involves leptomeninges and CSF

- Meningitis is inflammation of the leptomeninges and subarachnoid cerebrospinal fluid.
- Pyogenic meningitis is an acute, predominantly bacterial form.
- Meningococcal infection is an important etiology, especially in adolescents and young adults.

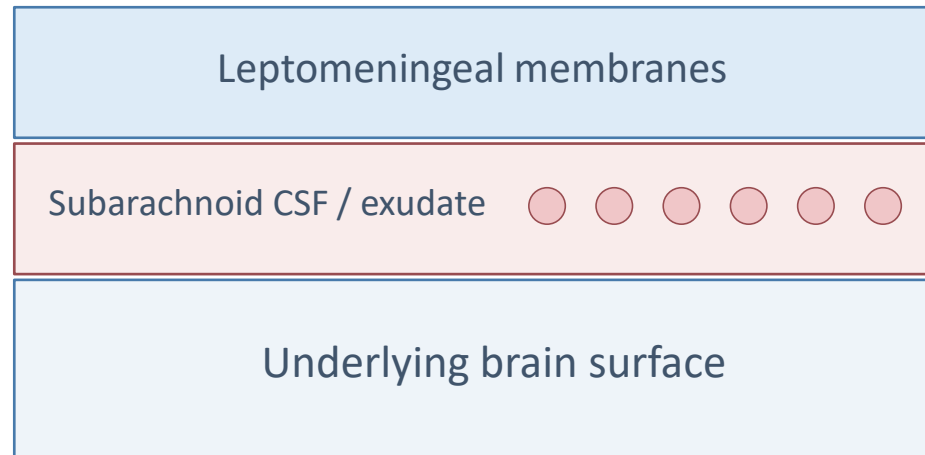
Clinical meningeal irritation and systemic infection

- Headache, photophobia and neck stiffness reflect meningeal irritation.
- Irritability or altered consciousness can accompany neurologic impairment.
- Systemic infection may coexist with severe CNS inflammation.

CSF findings distinguish pyogenic from aseptic meningitis

Characteristic	Acute pyogenic	Usually aseptic / viral
Appearance	Cloudy or purulent	Not typically frankly purulent
Predominant cells	Neutrophils	Lymphocytes
Protein	Increased	Usually moderate increase
Glucose	Markedly reduced	Usually normal

Pyogenic meningitis: Site of the exudate



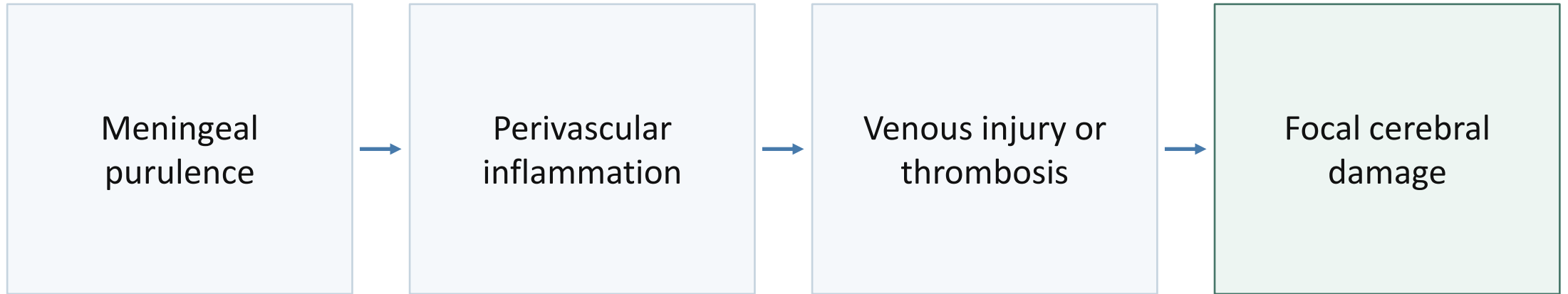
Anatomic schematic, not histology

- Suppurative exudate accumulates within leptomeningeal spaces.
- The meningeal vessels become engorged.
- The underlying brain parenchyma is not the primary compartment in uncomplicated meningitis.

Microscopy: Neutrophils occupy subarachnoid spaces

- Neutrophils fill subarachnoid spaces in severe acute bacterial meningitis.
- Less extensive inflammation is concentrated around leptomeningeal vessels.
- Gram staining can reveal organisms, particularly before antimicrobial treatment.

Extension of severe meningeal inflammation



Fulminant infection may progress to ventriculitis, vasculitis or cerebral infarction.

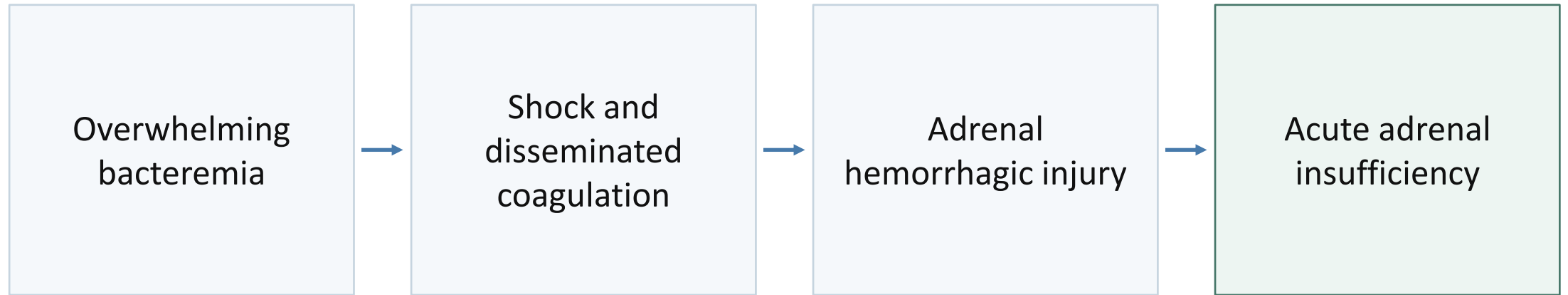
Healing can leave permanent meningeal sequelae

- Leptomeningeal fibrosis may follow a pyogenic inflammatory episode.
- Adhesions can interfere with CSF circulation and contribute to hydrocephalus.
- An acute bacterial infection can therefore produce delayed structural consequences.

Meningococcemia produces systemic consequences

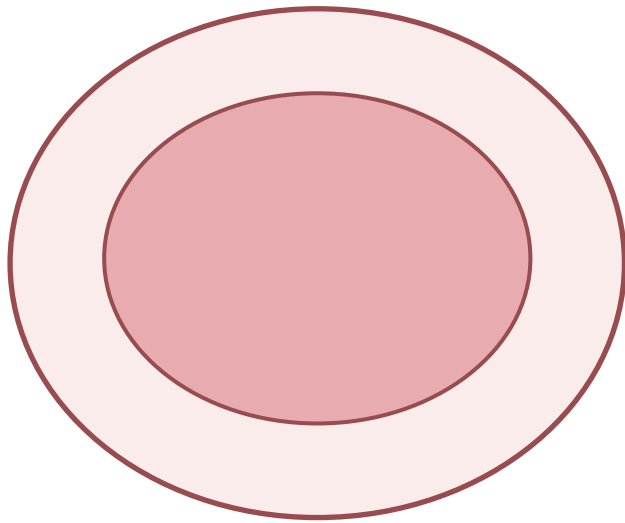
- Bloodstream infection may progress rapidly when complement defenses fail.
- Septicemia can be accompanied by widespread purpuric skin lesions.
- The most severe end of the spectrum includes shock, coagulopathy and adrenal hemorrhage.

Waterhouse–Friderichsen: Vascular catastrophe



Meningococcemia is the classic bacterial setting for this syndrome.

Waterhouse–Friderichsen: Adrenal morphology



Hemorrhage distorts tissue

Schematic organ section, not gross specimen

- Massive bilateral adrenal hemorrhage obscures normal adrenal architecture.
- Hemorrhage can begin near medullary venous sinusoids and extend into cortex.
- The initiating vascular mechanism is not established with certainty.

Case: Meningitis in a crowded residence

A young adult living in a dormitory develops fever, neck stiffness and rapidly worsening consciousness.

- Which organism matches this exposure and syndrome?
- Which anatomic barrier must be crossed before bloodborne CNS invasion?
- Which host defense defect would especially increase the risk?

Gonococcal disease starts at exposed mucosa

- *N. Gonorrhoeae* primarily infects urogenital, pharyngeal and anorectal mucosal sites.
- Local disease may be symptomatic or clinically silent.
- The key clinical danger is progression beyond an initially limited mucosal infection.

Gonococcal infection across anatomic sites

Site	Common manifestation	Potential concern
Male urethra	Urethritis	Upward spread in selected patients
Cervix	Cervicitis / silent infection	Ascending pelvic inflammatory disease
Pharynx	Local or occult infection	Persistence, treatment difficulty
Anorectum	Mucosal infection	May escape detection without site-based testing

Urethritis: Local inflammation in males

- Gonococcal urethritis represents an inflammatory response at the urethral mucosa.
- The disease is initially local rather than systemic.
- Ascending infection can contribute to epididymal inflammation in sexually active patients.

Epididymitis can follow ascending genitourinary infection

- In sexually active younger males, gonorrhea and chlamydia are important epididymitis pathogens.
- Acute epididymal inflammation features edema, congestion and neutrophilic infiltrates.
- Severe cases can evolve toward suppurative injury and later scarring.

Clinically silent cervical infection matters

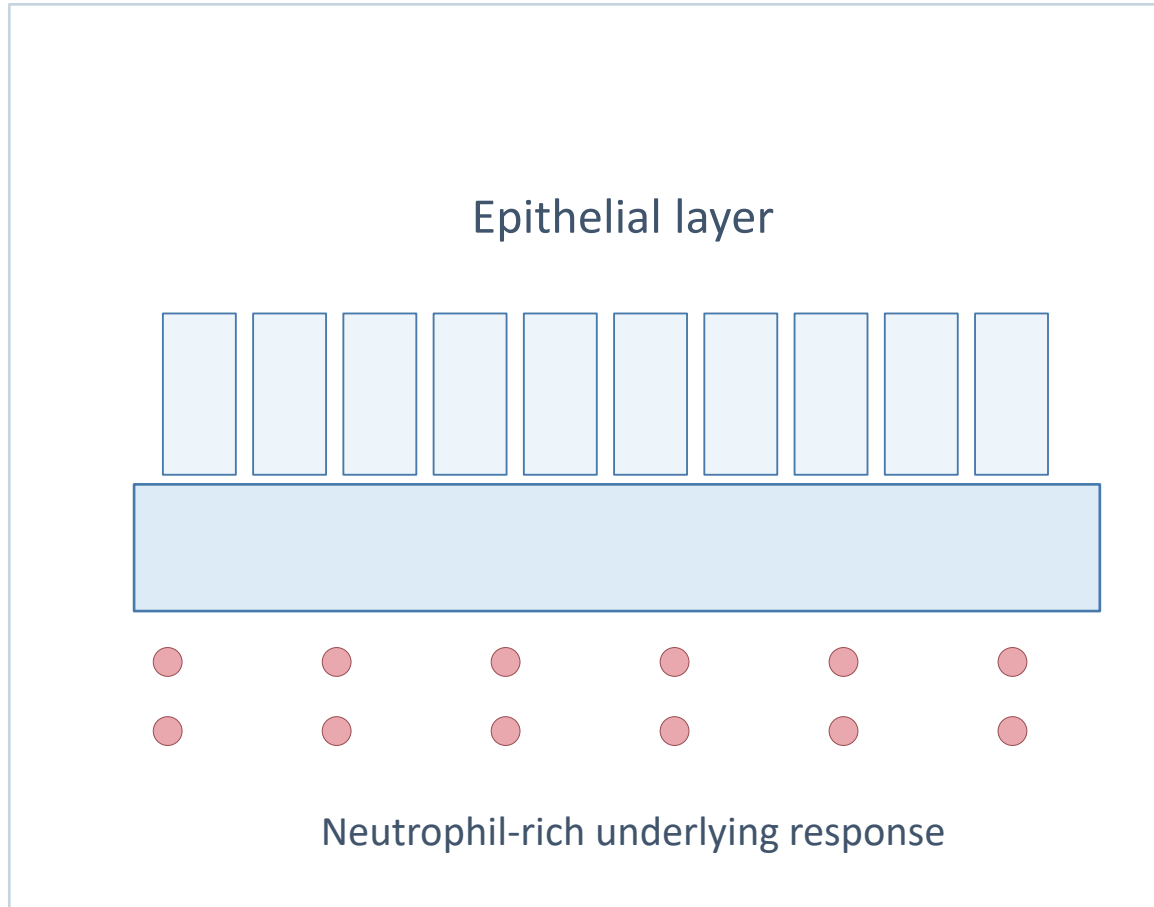
An asymptomatic infection can still be biologically active and capable of upward extension.

That gonorrhea in females may go unnoticed before PID or reproductive sequelae develop.

Endocervical mucosa is an important initial site

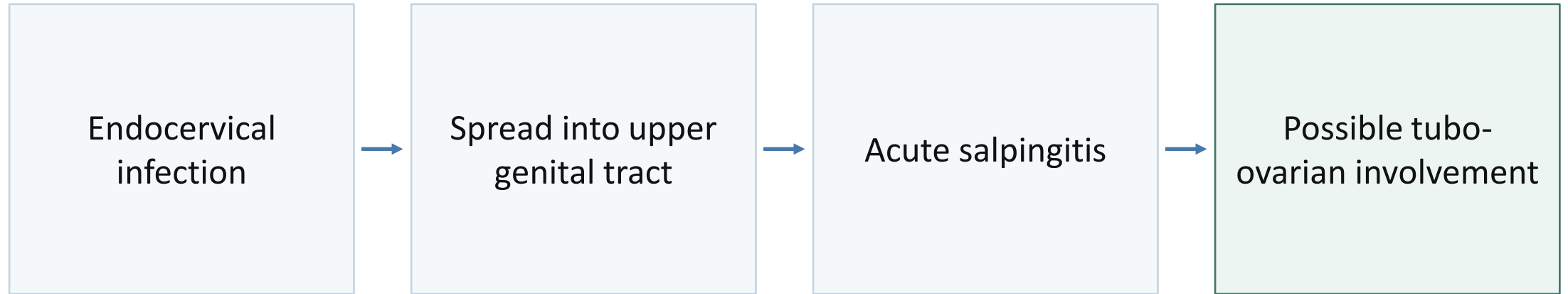
- Gonococcal pelvic infection commonly begins at the endocervix.
- Vestibular, periurethral and Bartholin glands can also be involved.
- Ascending organisms may then reach the fallopian tubes and tubo-ovarian region.

Mucosal inflammation: An epithelial and neutrophil response



- Gonococcal infection produces marked acute inflammation of mucosal surfaces.
- Purulent exudate reflects prominent neutrophilic recruitment.
- Epithelial damage provides a pathway for superficial spread.

Ascending gonococcal pelvic infection

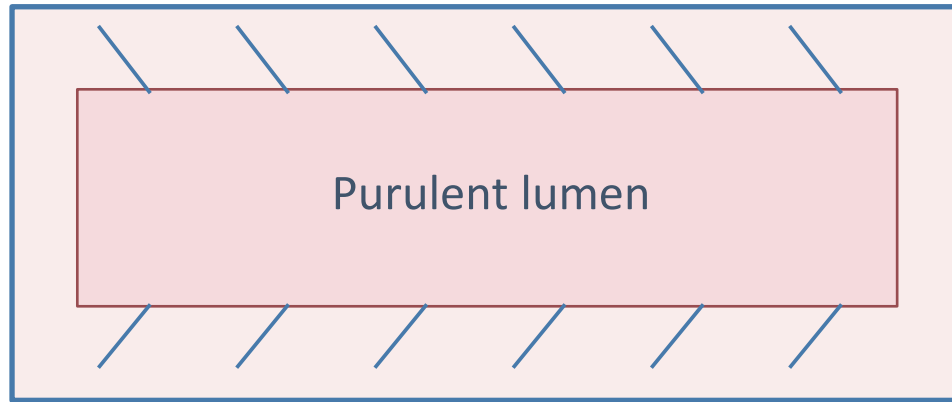


The mucosal surface is the characteristic route of upward spread.

Pelvic inflammatory disease is anatomically extensive

- PID comprises infection extending from lower genital sites into upper genital structures.
- Pelvic pain, adnexal tenderness, fever and vaginal discharge may accompany it.
- Gonococcus is one important cause, but PID is not exclusively gonococcal.

Acute salpingitis: The tube becomes suppurative



Simplified tubal cross-section · schematic

- The tubal mucosa is congested and infiltrated by neutrophils.
- Injury and sloughing of mucosal plicae can accompany acute infection.
- Purulent exudate accumulates in the tubal lumen.

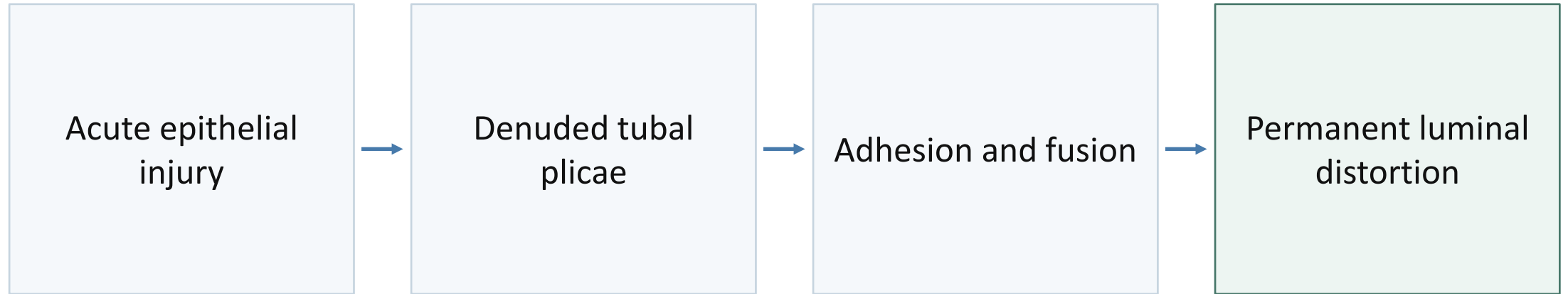
Pyosalpinx is purulent tubal distension

- Pus trapped in the fallopian-tube lumen produces pyosalpinx.
- Purulent material can also escape through the fimbrial end.
- These changes reflect the combination of mucosal injury and ongoing exudation.

Upper-tract complications occupy distinct spaces

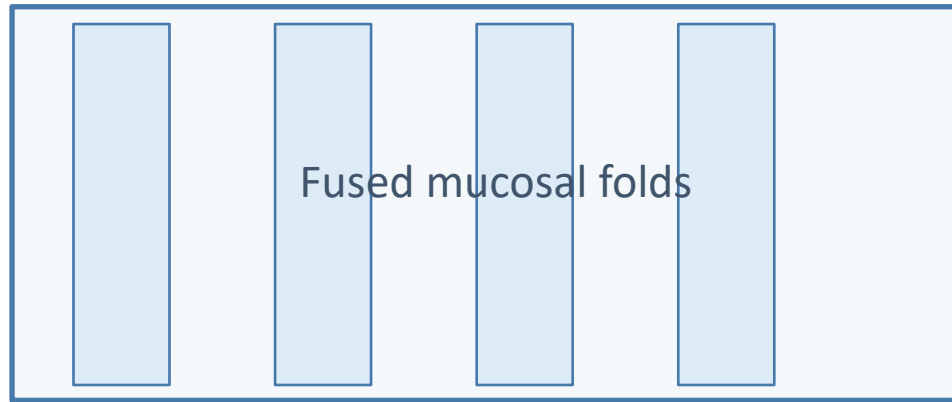
Lesion	Location	Pathologic feature
Acute salpingitis	Tubal mucosa and lumen	Neutrophils and purulent exudate
Pyosalpinx	Tubal lumen	Accumulated pus
Salpingo-oophoritis	Tube and adjacent ovary	Extension of inflammation
Tubo-ovarian abscess	Tube / ovary	Localized collection of pus

Repair after acute salpingitis can become destructive



Chronic tubal pathology may remain after organisms have disappeared.

Chronic salpingitis: Fused plicae create blind spaces



Simplified tubal cross-section · schematic

- Opposing mucosal folds adhere and fuse during healing.
- Scar-associated spaces may resemble glands or blind pouches.
- The distorted lumen loses normal transport function.

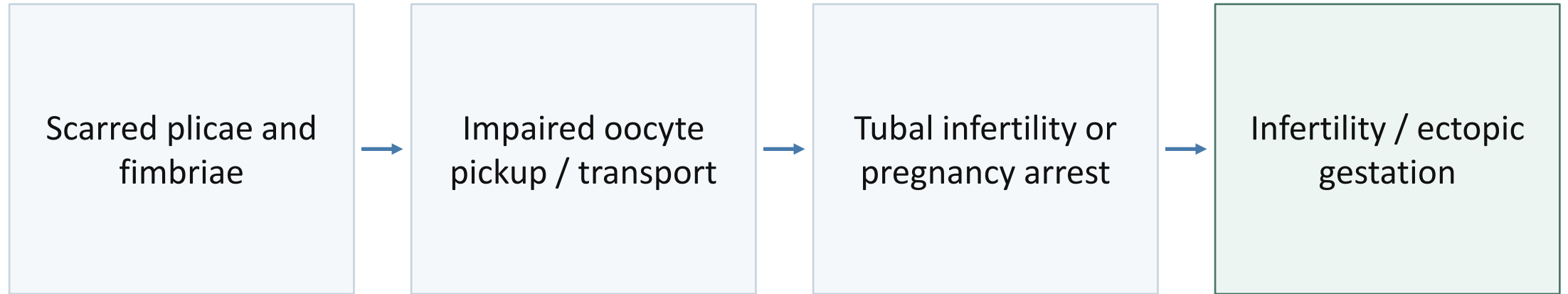
Hydrosalpinx: Distal closure retains secretions



Simplified tubal cross-section · schematic

- Fusion of the fimbriae obstructs normal outflow.
- Tubal secretions accumulate proximal to the blocked end.
- Distension produces a hydrosalpinx rather than a pus-filled pyosalpinx.

Tubal scarring explains reproductive outcomes



Morphology provides the causal link between earlier infection and later complications.

Gonococcal versus other bacterial PID patterns

Feature	Gonococcal PID	Postpartum / postprocedural PID
Spread	Predominantly ascending mucosal	May use lymphatic / venous routes
Dominant early injury	Mucosa / tube lumen	Deeper tissue layers may predominate
Microbiology	Gonococcus as etiologic agent	Often polymicrobial
Tissue pattern	Acute suppurative salpingitis	May involve serosa and adjacent structures

Laboratory diagnosis: Detection of organismal material

- Nucleic-acid amplification testing as a primary gonorrhea diagnostic approach.
- Culture remains an alternative and can be important when organism recovery is needed.
- Neutrophils containing gram-negative diplococci are suggestive on smear but do not replace definitive testing.

Pharyngeal infection creates a therapeutic challenge

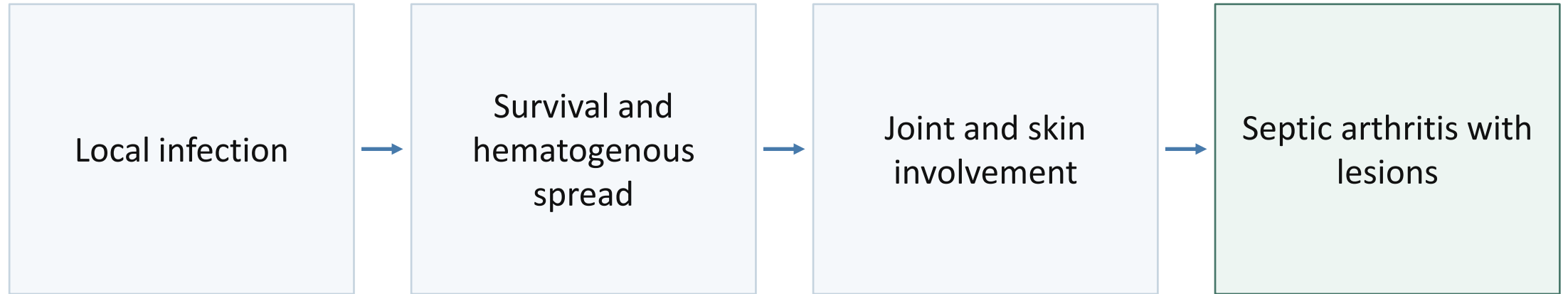
- The oropharynx is a possible site of gonococcal infection.
- Unsuccessful treatment of resistant infection particularly with throat involvement.
- Antimicrobial penetration and emerging resistance complicate management; Specific current regimens require an up-to-date guideline.

Antimicrobial resistance is a moving target

Resistance to cephalosporins is a documented concern for *N. Gonorrhoeae*.

This pathology lecture does not reproduce the textbook's historical drug combination as current prescribing guidance.

Disseminated gonococcal infection leaves the mucosa



Dissemination is less frequent than localized mucosal disease.

Disseminated disease combines arthritis with skin lesions

- Septic arthritis as a common disseminated manifestation.
- Hemorrhagic papules and pustules can accompany the joint process.
- The clinical combination should prompt consideration of gonococcal infection, even when mucosal symptoms are absent.

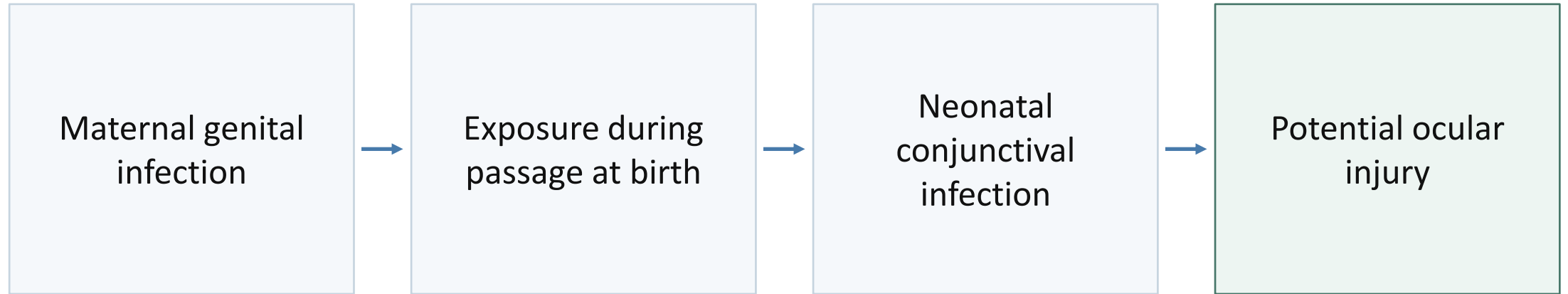
Terminal complement also restrains gonococcal spread

- People lacking membrane attack complex proteins are predisposed to disseminated gonococcal infection.
- This common host factor links meningococcal and gonococcal invasive disease.
- The usual expression of dissemination still differs between the two species.

Neonatal gonococcal disease threatens vision

- Gonococcus may infect the neonatal conjunctiva during birth.
- Severe neonatal conjunctivitis can damage the eye and lead to blindness.
- Rare neonatal sepsis is also.

Perinatal conjunctivitis: Sequence of events



The neonatal infection reflects contact during delivery, not inherited disease.

Prevention of neonatal eye disease is time-sensitive

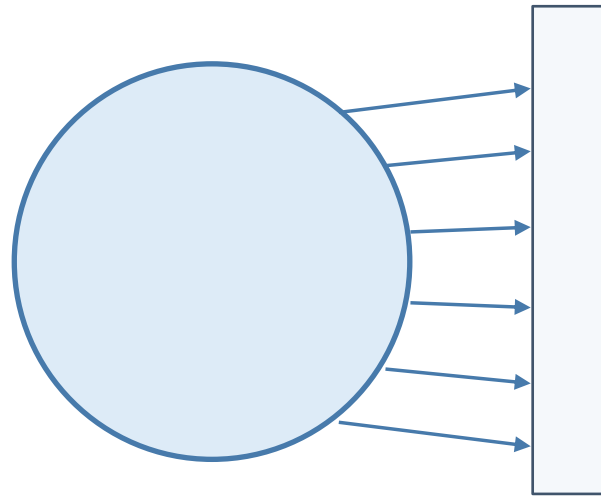
- Ocular prophylaxis with instilled agents at birth.
- The rationale is prevention of destructive neonatal conjunctival infection.
- Choice of agent and local protocol should follow current obstetric and public-health guidance.

Case: Quiet cervicitis, delayed infertility

A patient has a history of minimally symptomatic cervical infection and later presents with tubal-factor infertility.

- What upper-tract complication could have occurred?
- What morphologic change persists after organisms are cleared?
- Why can the resulting lesion interfere with fertility?

Pili mediate initial epithelial attachment



Long pili: First attachment
Schematic bacterium / epithelium

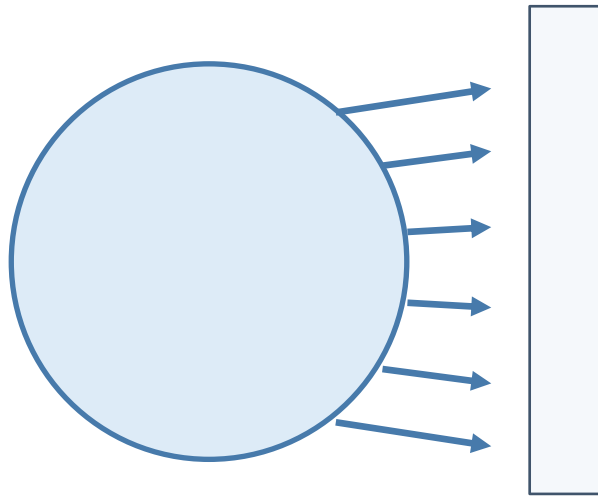
- Long pili make the initial contact with epithelial surfaces.
- For *N. Gonorrhoeae*, CD46 as a pilus-binding host molecule.
- Attachment is an early requirement for subsequent superficial invasion.

CD46 is the cited host attachment molecule

Pili binding CD46 on human nucleated cells.

The slide records the molecular relationship given in the supplied text; It does not imply CD46 is the sole Neisseria receptor.

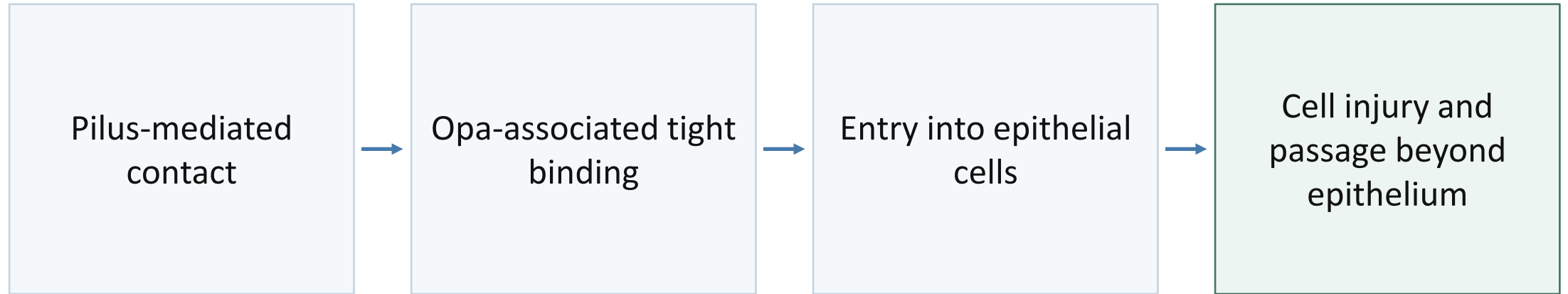
Opa proteins strengthen attachment and entry



Outer-membrane Opa: Tighter binding
Schematic bacterium / epithelium

- Outer-membrane Opa proteins increase epithelial binding.
- They promote entry of organisms into epithelial cells.
- The name derives from the opaque colony phenotype.

The epithelial invasion sequence

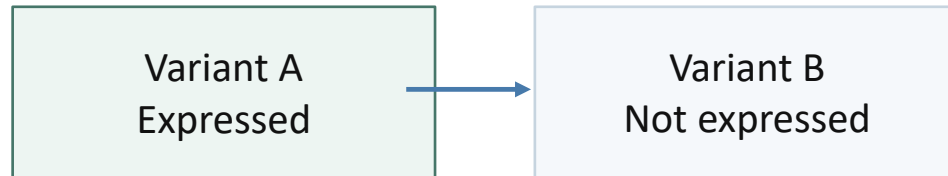


This sequence explains why a mucosal infection is not simply passive surface colonization.

Antigenic variation changes what immunity recognizes

- A single bacterial clone may alter the antigens it expresses.
- The source identifies pilus-related recombination and changes in Opa expression.
- Changing surface antigens can help the organism escape an existing immune response.

Pilin gene recombination changes expressed pili

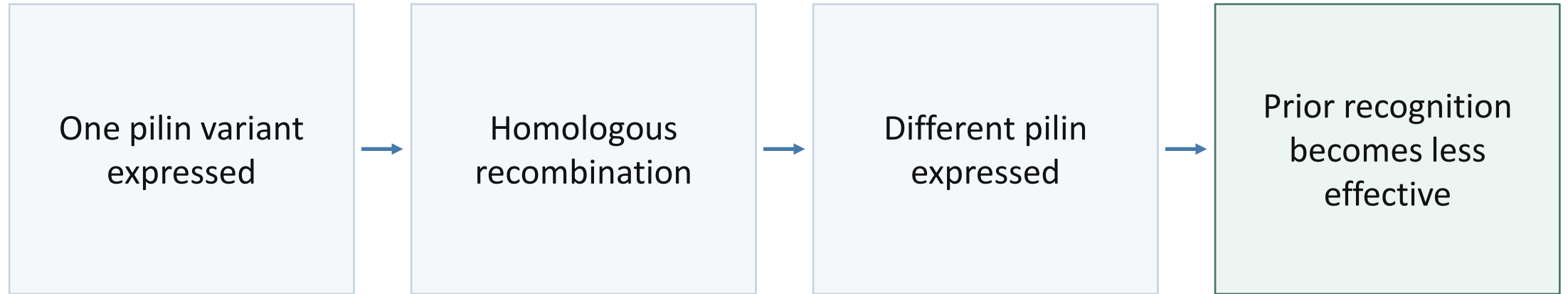


Recombination
Changes active variant

Schematic concept, not a gene map

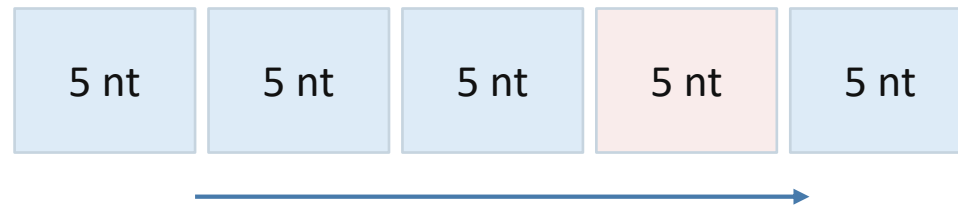
- Alternative pilin coding sequences exist within the genetic repertoire.
- Homologous recombination shifts the variant that is expressed.
- A new pilus antigen can emerge without replacement of the bacterial clone.

Pilus antigen change alters the host–pathogen interaction



The antigenic phenotype of a clone can change over time.

Opa repeat changes can alter protein expression



Repeat gain / loss

Reading-frame change → protein variation

- The source describes short five-nucleotide repeat sequences in OPA genes.
- Repeat gain or loss shifts the reading frame and may introduce stop codons.
- These changes alter which Opa products are expressed.

Two distinct antigenic-variation mechanisms

Dimension	Pilus system	Opa system
Primary genetic event	Homologous recombination	Repeat gain / loss
Immediate effect	Different expressed pilin	Reading-frame changes
Changed surface feature	Pilus antigen	Opa protein repertoire
Biologic advantage	Reduced immune recognition	Reduced immune recognition

Antigenic variation and capsular diversity are distinct

- Meningococcal capsular serogroups describe differences between strains.
- Pilus and Opa variation can change expression within a bacterial lineage.
- Both affect immune recognition, but operate at different biological levels.

Syndrome comparison: A practical diagnostic framework

Feature	Meningococcal infection	Gonococcal infection
Primary setting	Nasopharyngeal exposure	Mucosal sexual / perinatal exposure
Typical pathology	Pyogenic meningitis; Septicemia	Mucosal inflammation; Salpingitis
Disseminated lesion	Sepsis $\pm$ adrenal hemorrhage	Arthritis $\pm$ skin pustules
Unifying risk	Terminal complement defects	Terminal complement defects

Organ pathology connects to clinical consequences

Structure	Injury	Consequence
Subarachnoid space	Neutrophilic exudate	Meningeal irritation / CNS dysfunction
Adrenal glands	Massive hemorrhage	Acute adrenal insufficiency
Tubal plicae / fimbriae	Suppuration followed by fibrosis	Infertility / ectopic pregnancy
Neonatal conjunctiva	Acute infection	Visual injury

Case: Recurrent invasive *Neisseria* infections

A patient has a history of severe meningococcal infection and later a disseminated gonococcal illness.

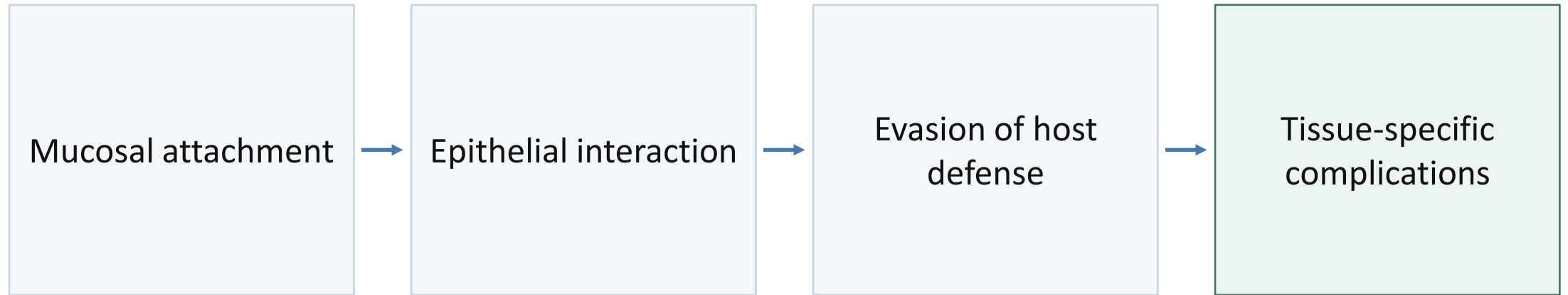
- Which common immune effector system deserves scrutiny?
- What molecular components constitute the terminal system?
- Why are these otherwise different infections linked?

Case: Joint swelling and pustular eruption

A sexually active adult develops acute arthritis and several hemorrhagic papules and pustules, with little local genital symptomatology.

- Which gonococcal manifestation is plausible?
- Does absent urethral or cervical pain exclude this infection?
- Which host defect would strengthen the suspicion?

Integrated model: Two species, one set of mechanisms



Clinical phenotype depends on the organism, site of entry, and host immunity.

Clinicopathologic synthesis

- Meningococci: Oropharyngeal carriage can progress through blood to acute pyogenic meningitis.
- Gonococci: Mucosal infection can ascend, scar the fallopian tubes, or occasionally disseminate.
- Pili, Opa proteins and antigenic variation connect epithelial pathogenesis to immune escape.
- Terminal complement C5–C9 is a shared protective system against invasive Neisseria disease.

Textbook sources for further reading

- Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th edition (2026): Infectious Diseases — Neisserial Infections.
- Related sections: Central Nervous System — Acute Pyogenic Meningitis; Female Genital Tract — Pelvic Inflammatory Disease.
- Related sections: Adrenal Glands — Waterhouse–Friderichsen Syndrome; Male Genital Tract — Epididymitis and Orchitis.