5th Conference of STP-I

Spontaneous and induced lesions of the gastrointestinal tract

- INHAND nomenclature and diagnostic critiera (II) -

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INHAND:
Digestive Tract Organ Working Group

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Lesions to be presented

All organs of the digestive tract

- Infiltrate vs. inflammation
- Single cell necrosis/apoptosis, necrosis

Pancreas

- Degranulation, acinar cell
- Atrophy, acinar cell
- Metaplasia, ductular

Salivary glands

- Tumor, mixed, malignant
- Myoepithelioma, malignant

Gastrointestinal tract

- Leiomyoma
- Gastrointestinal Stromal Tumor (GIST)

Salivary glands, pancreas

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Infiltrate

Modifiers:

Type of inflammatory cell that represents the predominant cell type in the infiltrate

Pathogenesis:

Infiltration with neutrophils (Infiltrate, neutrophil), eosinophils (Infiltrate, eosinophil), mononuclear cells (Infiltrate, mononuclear cell) or a combination of more than one type (Infiltrate, mixed) present without other morphological features of inflammation, e.g. hemorrhage, edema, fibroplasia.

Diagnostic key features:

- Focal, multifocal or diffuse.
- Presence of mononuclear or polymorphonuclear leukocytes but without other histological features of inflammation like edema, congestion or necrosis.
- Usually no acinar cell degranulation or mucus depletion.

Salivary glands

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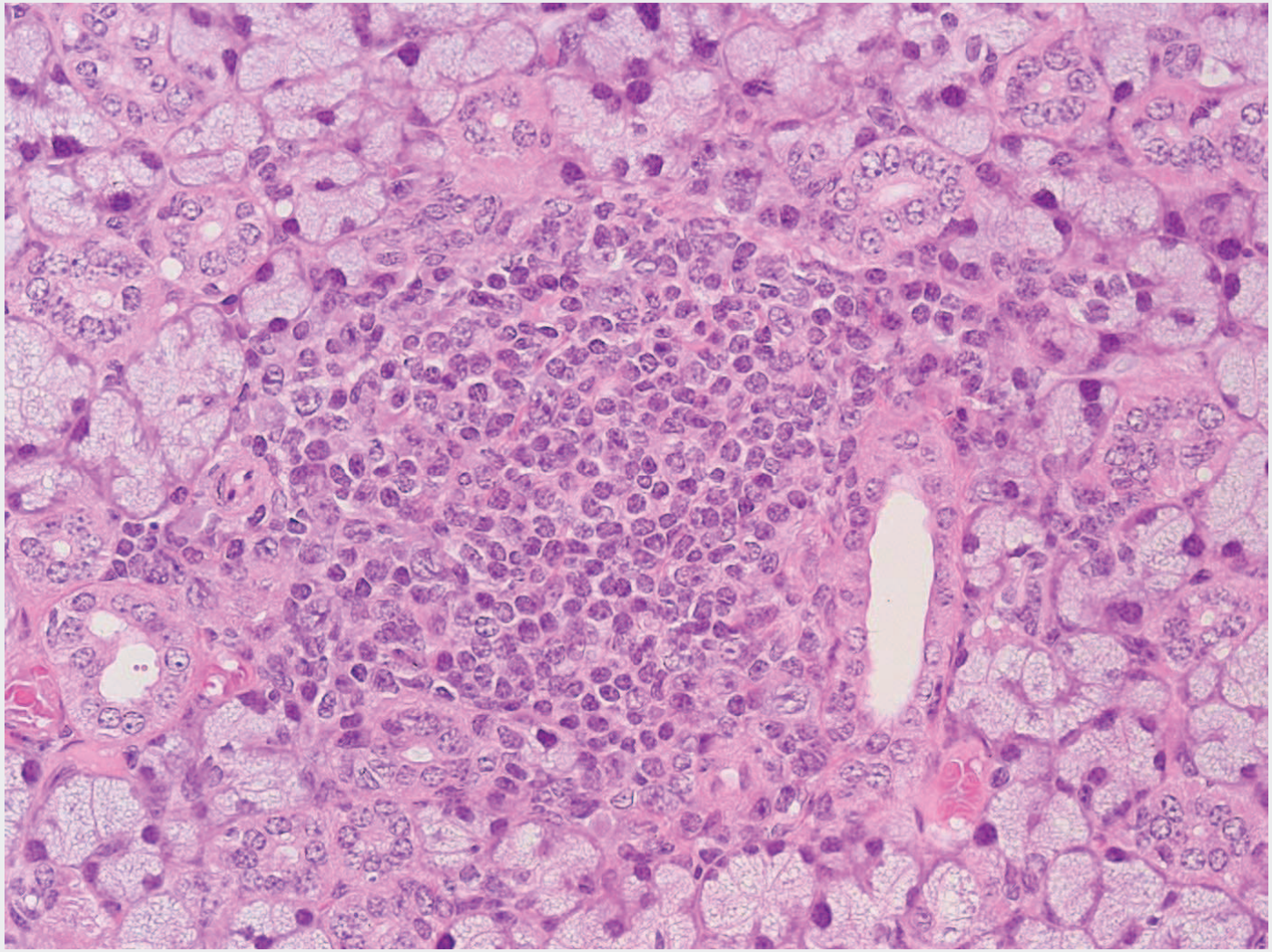
Infiltrate, mononuclear cell



Salivary glands, pancreas

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Inflammation

Modifier:

Type of inflammatory cell that represents the predominant cell type in the inflammation

Pathogenesis:

Infiltration with neutrophils (Inflammation, neutrophil) or mononuclear cell (Inflammation, mononuclear cell) or a combination (Inflammation, mixed) with additional histological features of inflammation e.g. hemorrhage, edema, fibroplasia.

Diagnostic key features:

- Focal (salivary glands), focally extensive or diffuse, involving predominantly the interstitium, but also acinar cells and intra- or inter-lobular ducts.
- Infiltrate of mononuclear or polymorphonuclear leukocytes into the gland parenchyma.
- Presence of other histological criteria of inflammation, e.g. hemorrhage, edema, fibroplasias.

Salivary glands

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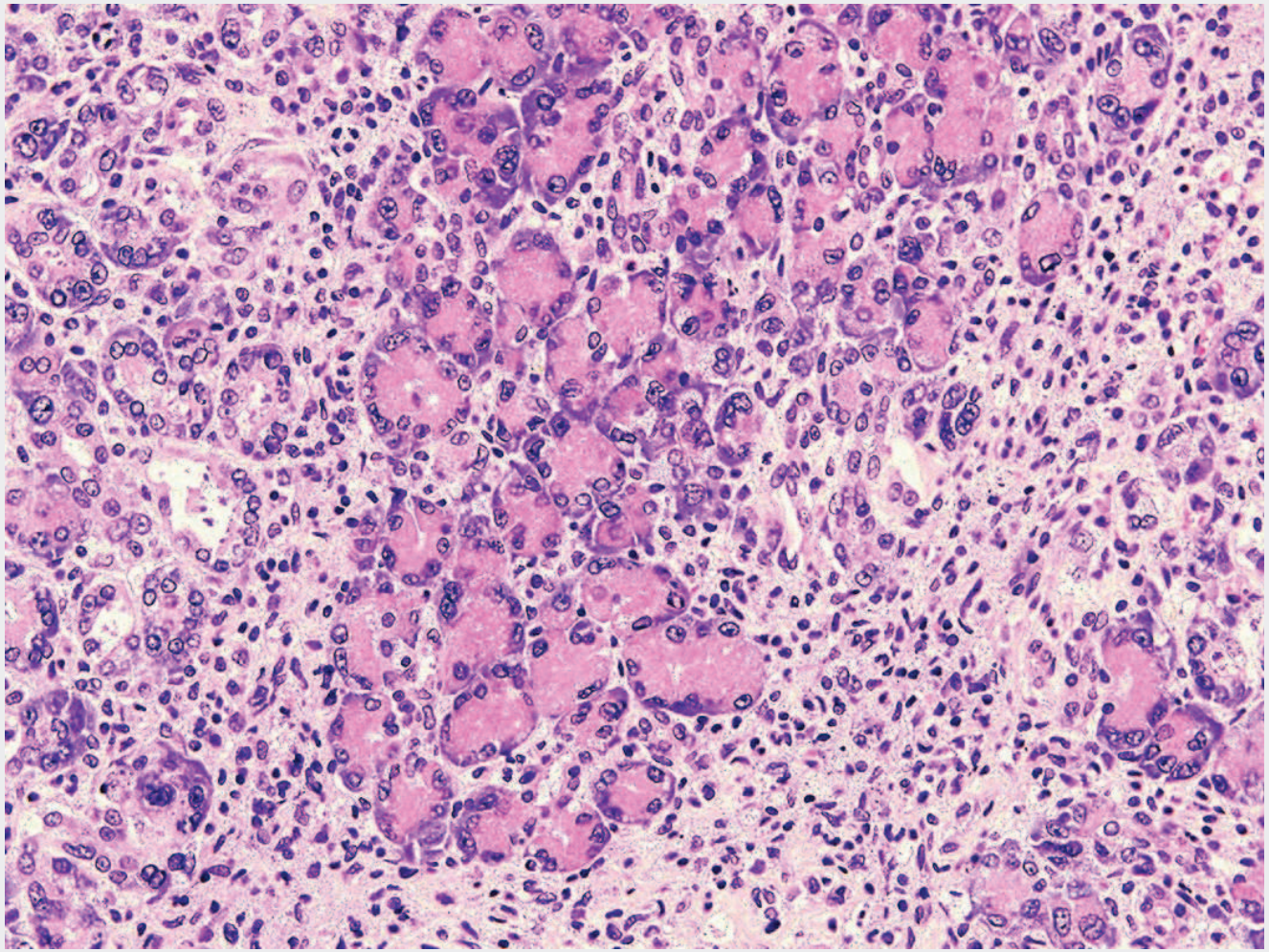
Inflammation, mononuclear cell



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Digestive tract, all parts

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Revision of cell death terminology

The starting point:

- Different approaches in different organ systems; examples:
  - Testis: Degeneration, germ cell – syn. Single cell necrosis, apoptosis
  - Kidneys, epididymis, accessory sex glands: Single cell necrosis – syn. Apoptosis
  - Integument: Recommendation not to use the term „apoptosis“ unless shown by special techniques; instead: Necrosis, single cell type
- In scientific community outside toxicologic pathology, strict differentiation between single cell necrosis and apoptosis; shared by several experts in different INHAND OWGs

→ INHAND-GESC concluded that single cell necrosis and apoptosis are not synonymous

→ INHAND-GESC established a Working group „Apoptosis/necrosis“ with the aim to re-address the nomenclature and diagnostic critieria of cell death in routine toxicologic pathology

Digestive tract, all parts

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Revision of cell death terminology

The approach of the INHAND necrosis/apoptosis Working Group – applied to the digestive tract (DRAFT):

Death of individual cells:

1. Single cell necrosis
2. Apoptosis
3. Single cell necrosis/apoptosis
   (death of individual cells that is not unequivocally single cell necrosis or apoptosis; or both single cell necrosis and apoptosis are present)

Death of groups of cells

4. Necrosis

Digestive tract, all parts

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Apoptosis

Pathogenesis:

Gene regulated, energy dependent process leading to formation of apoptotic bodies which are phagocytosed by adjacent cells.

Diagnostic key features:

- Single cell death or small clusters of cells.
- Cell shrinkage and convolution.
- Cytoplasmic condensation (hypereosinophilia).
- Chromatin condensation (pyknosis) and peripheralization in early apoptosis.
- Karyorrhexis with fragmentation of condensed chromatin.
- Intact cell membrane.
- Formation of blebs to produce apoptotic bodies.
- Cytoplasm retained in apoptotic bodies.
- Phagocytosis of apoptotic bodies tissue macrophages or other adjacent cells.
- Lack of inflammation.

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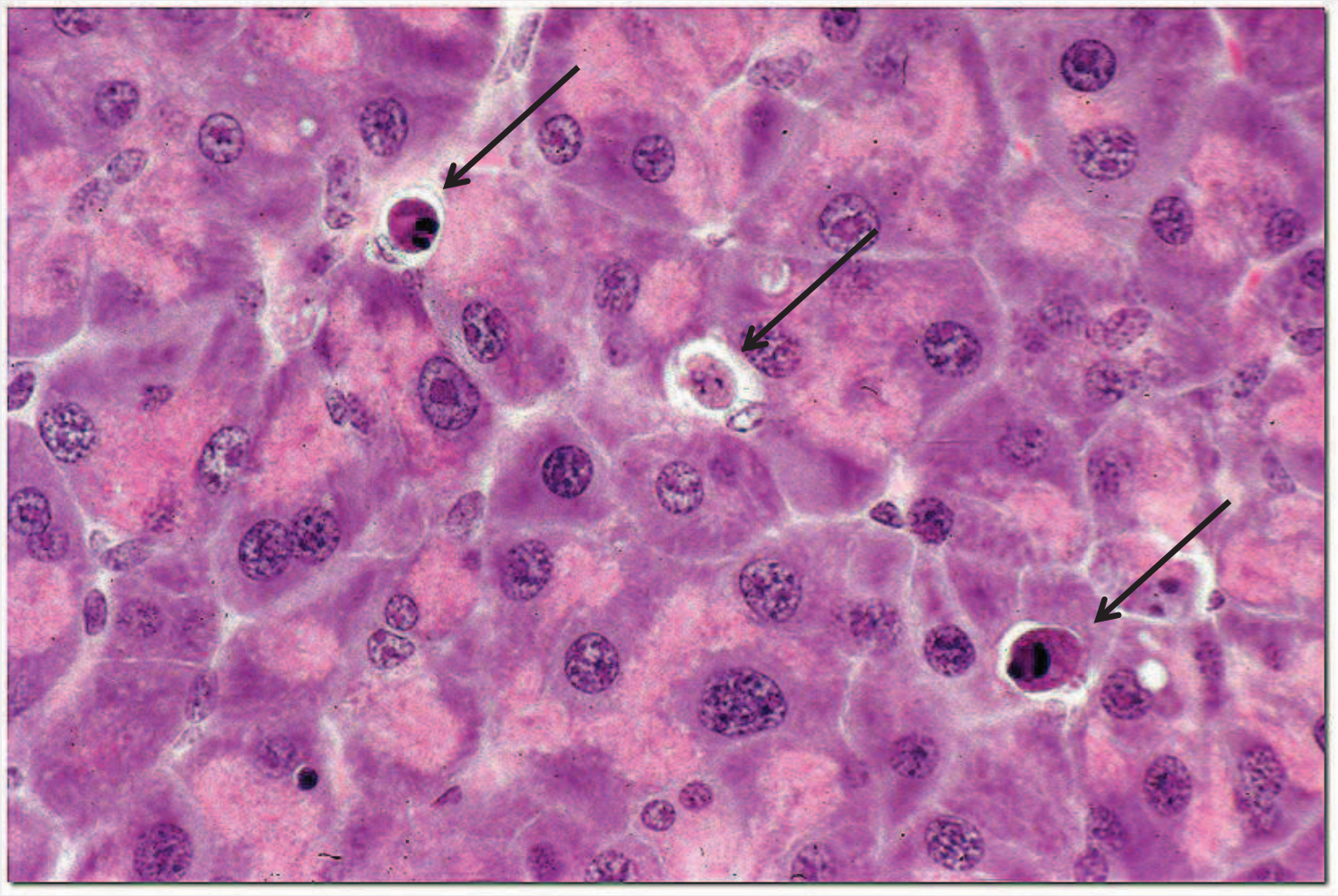
Apoptosis



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Digestive tract, all parts

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Single cell necrosis

Pathogenesis:

Unregulated, energy independent, passive cell death with leakage of cytoplasm into surrounding tissue and subsequent inflammatory reaction.

Diagnostic key features:

- Often contiguous cells.
- Cell and organelle swelling.
- Pyknosis (nuclear condensation: minor component).
- Karyorrhexis (nuclear fragmentation).
- Karyolysis (degradation of nuclear material).
- Cytoplasmic blebs.
- Plasma membrane rupture.
- Intracellular contents released into surrounding tissue.
- Inflammation usually present.

Pancreas

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Necrosis

Diagnostic key features:

- Focal, lobular, or diffuse.
- Swollen cells with eosinophilic flocculated cytoplasm.
- Early lesions may retain cellular outlines.
- Pyknotic or indistinct nuclei with loss of chromatin to total loss of nuclei.
- Inflammatory cell infiltrate, edema and fibrin may surround the necrotic cells, but necrosis is still predominant.
- Destruction of adjacent fat cells and fat necrosis in advanced and exaggerated stages.

Differential diagnoses:

- Single cell necrosis/apoptosis: Scattered, isolated cells affected, forming apoptotic bodies; or isolated swollen cells with plasma membrane rupture (single cell necrosis).
- Inflammation, acute: Infiltrates of inflammatory cells, edema, and fibrin predominate; necrosis may be present, but is a minor component.

Pancreas

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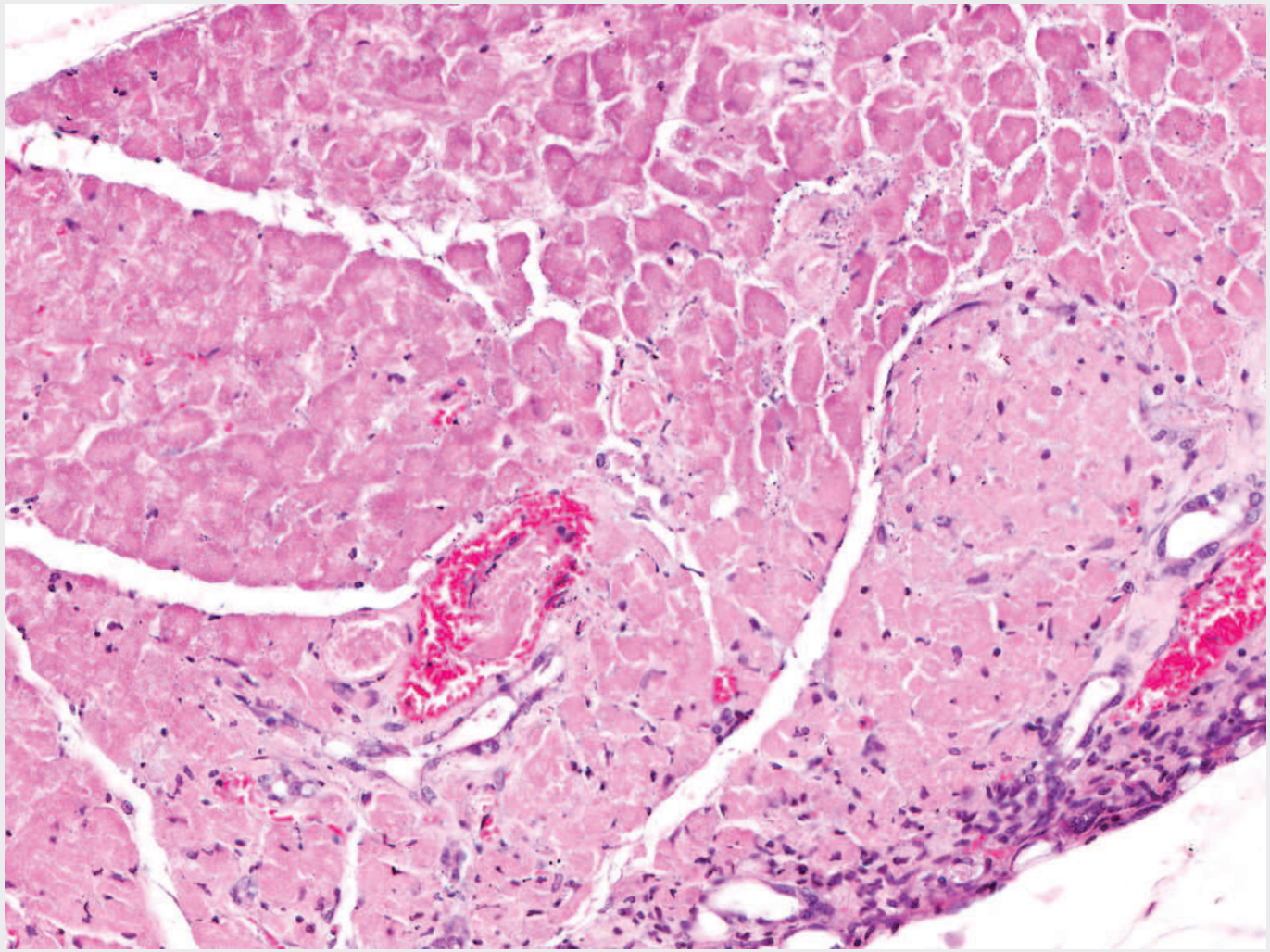
Necrosis



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Secretory depletion, acinar cell

Pathogenesis: Decrease of acinar cell zymogen granules leading to shrunken acinar cells with increased basophilia.

Diagnostic features

- Focal, lobular, or diffuse lesion.
- Reduced acinar diameter.
- Partial or complete loss of acinar cell zymogen granules leading to a reduced cell size and increased basophilia.
- Lack of fibrosis or adipocyte infiltration.
- Islets of Langerhans are unaffected.

Pancreas

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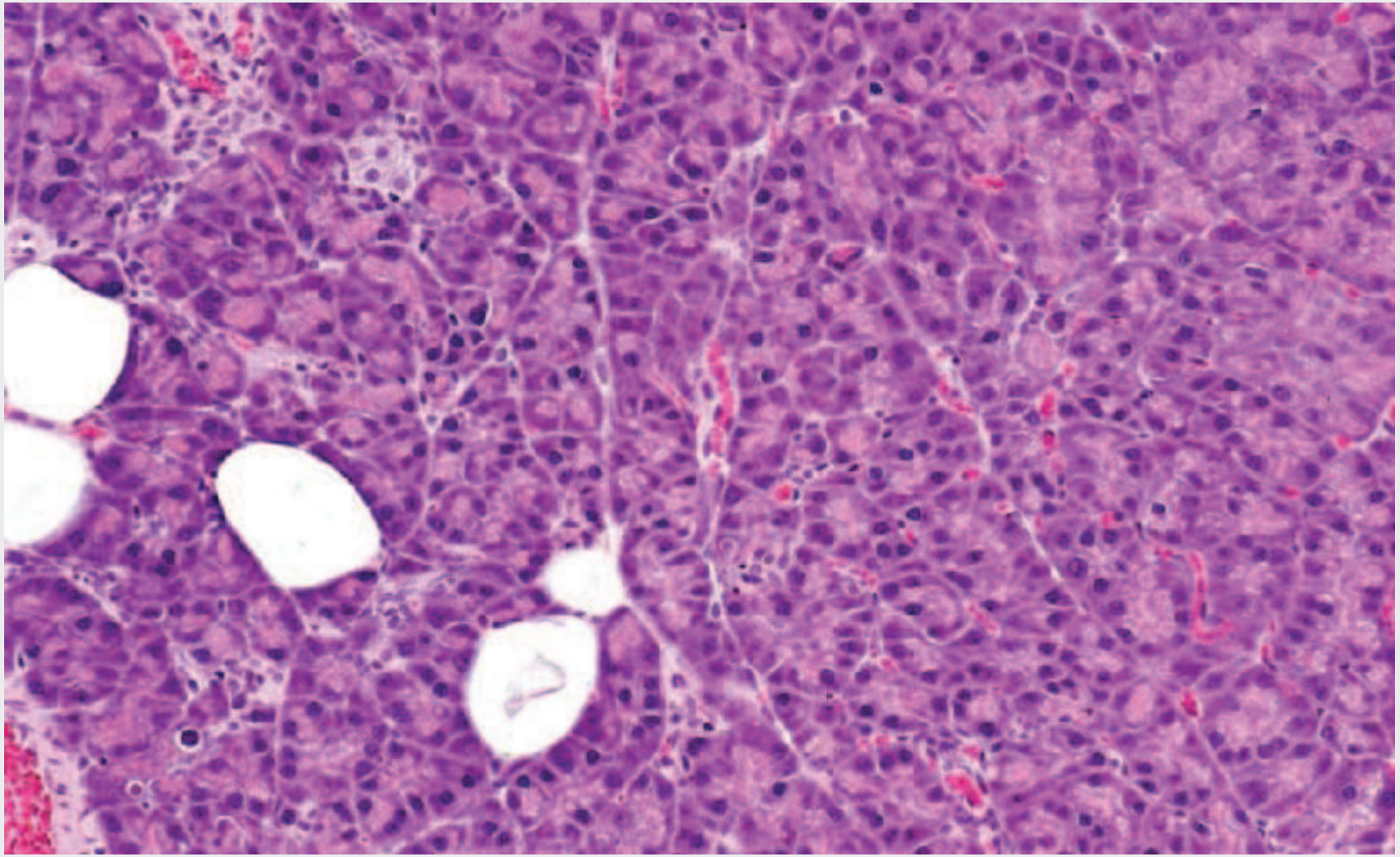
Secretory depletion, acinar cell



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Secretory depletion, acinar cell

Differential diagnoses:

Atrophy, acinar cell:
Loss of acinar cell basophilia and decreased zymogen granules resulting in small acini lined by **small columnar cells almost completely devoid of cytoplasm** and with a small and inactive nucleus; may be accompanied by fibrosis and minimal mononuclear cell infiltrates.

Peri-insular halos:

Tele-insular acinar cells have relatively less zymogen granules and more RER when compared to peri-insular acinar cells.

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Peri-insular halos

Synonyms: Eosinophilic change; focal eosinophilic hypertrophic cells

Pathogenesis: Hypertrophy of pancreatic exocrine acinar cells surrounding the Islets of Langerhans.

Diagnostic features:

- Hypertrophy of exocrine pancreatic acini surrounding the islets of Langerhans.
- Acinar cells with more abundant cytoplasmic volume with larger zymogen granules than tele-insular acinar cells (located distantly from the islets).
- Larger nuclei with more nucleoli than tele-insular acinar cells.

Pancreas

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Peri-insular halos