5th Conference of STP-I

Spontaneous and induced lesions of the gastrointestinal tract

- INHAND nomenclature and diagnostic critiera (I) -

Dr. Thomas Nolte, DVM, MSc, F.I.A.T.P.
Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach / Riss, Germany

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INHAND:
Some general aspects

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What is INHAND?

- International Harmonization of Nomenclature and Diagnostic Criteria for Lesions in Rats and Mice
- Joint initiative of societies in Toxicologic Pathology: BSTP, ESTP / RITA, JSTP STP

INHAND objectives:

- Generation of standardized nomenclature and diagnostic criteria for lesions in rats and mice, and subsequently non-rodents
- Publication per organ system in “Toxicologic Pathology” or “Journal of Toxicologic Pathology”
- Change-control established
- Actual on-line versions: goRENI (www.goreni.org)
- goRENI account may be granted to any member of a society of toxicologic pathology

INHAND:
Some general aspects

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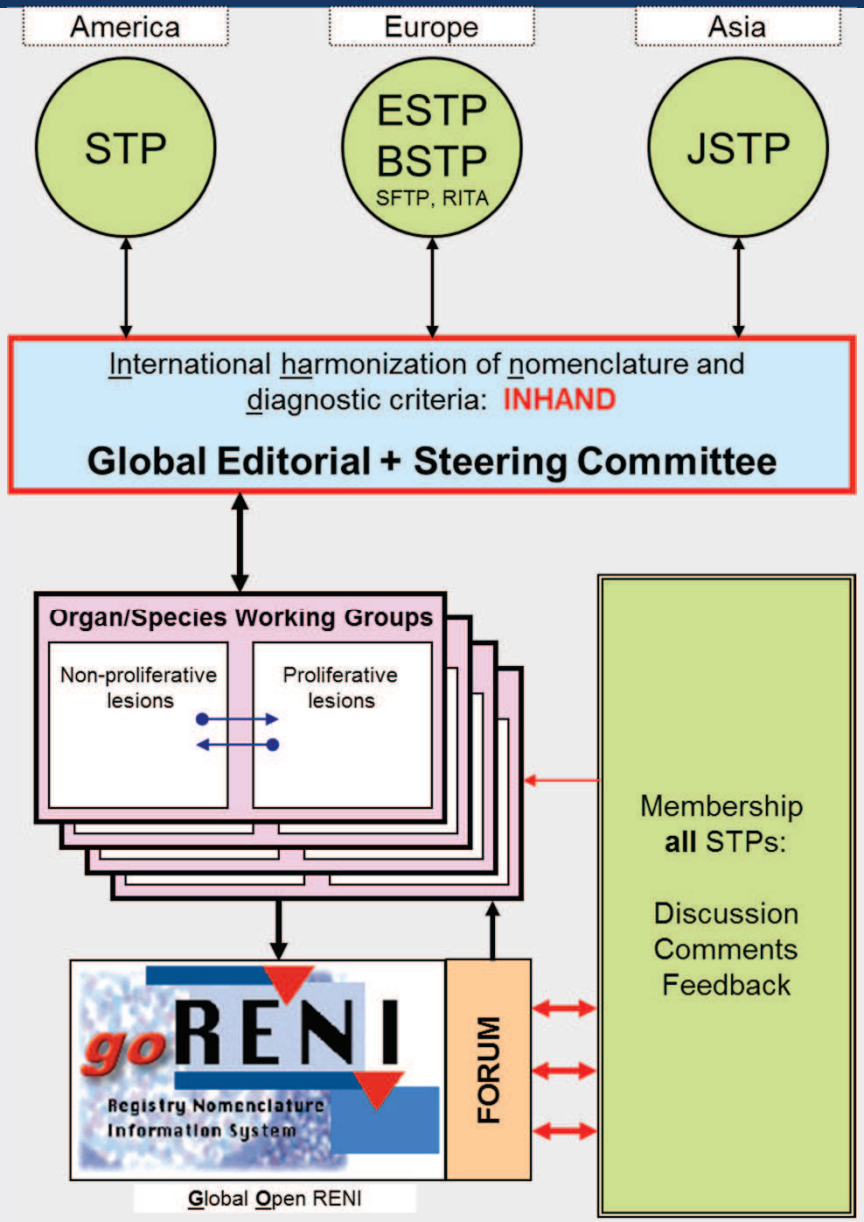
The structure of INHAND

- Global Executive Steering Committee (GESC) with representation from major societies of toxicologic pathology
- 15 Organ system Working Groups (OWGs)
- 4 non-rodent species working groups (dog, minipig, monkey, rabbit)
- Working group on apoptosis / necrosis
- Each working group composed of experts in the field from each of the participating societies

INHAND and US-FDA SEND

- GESC and OWGs serve in advisory role with the goal of mapping INHAND terminology to SEND codelists of preferred terms

INHAND: Organization



INHAND:
Some general aspects

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INHAND principles

- Include
  - Lesions in rats and mice (non-rodents just started)
  - Non-proliferative and proliferative lesions
  - Spontaneous and induced lesions
- Terminology descriptive rather than diagnostic (“vacuolation” – not “phospholipidosis”)
- Diagnostic criteria based on H&E morphology (“pigment” rather than “lipofuscin”)
- Use of lesion terms instead of process terms (“ulcer” rather than “ulceration”)

INHAND:
Some general aspects

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Completed organ systems:

- Respiratory (Toxicol Pathol. 37 (7 Suppl):5S-73S)
- Hepatobiliary (Toxicol Pathol. 38(7 Suppl): 5S-81S)
- Urinary (Toxicol Pathol. 40 (4 Suppl): 14S-86S)
- CNS/PNS (Toxicol Pathol. 40 (4 Suppl): 87S-157S)
- Mammary, Zymbal's, Preputial and Clitoral Glands (Toxicol Pathol. 40(6 Suppl): 7S-39S)
- Male Reproductive (Toxicol Pathol. 40(6 Suppl): 40S-121S)
- Soft Tissue (J Toxicol Pathol. 26 (3 Suppl): 1S-26S)
- Integument (J Toxicol Pathol. 26 (3 Suppl): 27S-57S)

In progress:

- Female reproductive system (to be published in 2014)
- Digestive system (final draft)
- Cardiovascular system (in review)
- Lymphoid and hematopoietic system
- Skeletal system
- Endocrine system
- Special senses
- Non-rodent
- Apoptosis / necrosis

INHAND:
Digestive Tract Organ Working Group

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Status

- Final draft manuscript:
  - Review by society members done
  - Review and implementation of membership comments ongoing
- Publication scheduled for 2015 (after final review by GESC)

Aim of this presentation

- Presentation of diagnostic challenges / new concepts / controversial lesions
- Emphasize will be on key differential diagnostic criteria

INHAND:
Digestive Tract Organ Working Group

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Lesions to be presented

- Basal cell hyperplaisa of the nonglandular stomach
- Proliferative mucosal lesions of glandular stomach / intestine
    - Diverticulum
    - Hyperplasia (mucosal)
    - Adenoma
    - Adenocarcinoma

Nonglandular stomach

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Hyperplaisa, basal cell

Histogenesis: Basal layer of the stratified squamous epithelium

Diagnostic features

- Proliferation of the basal cell layer, basophilic staining increased.
- Focal or diffuse.
- Endophytic growth pattern.
- No alteration of basement membrane integrity.
- Papillary body shows marked undulation but rete peg structure still present.

Nonglandular stomach

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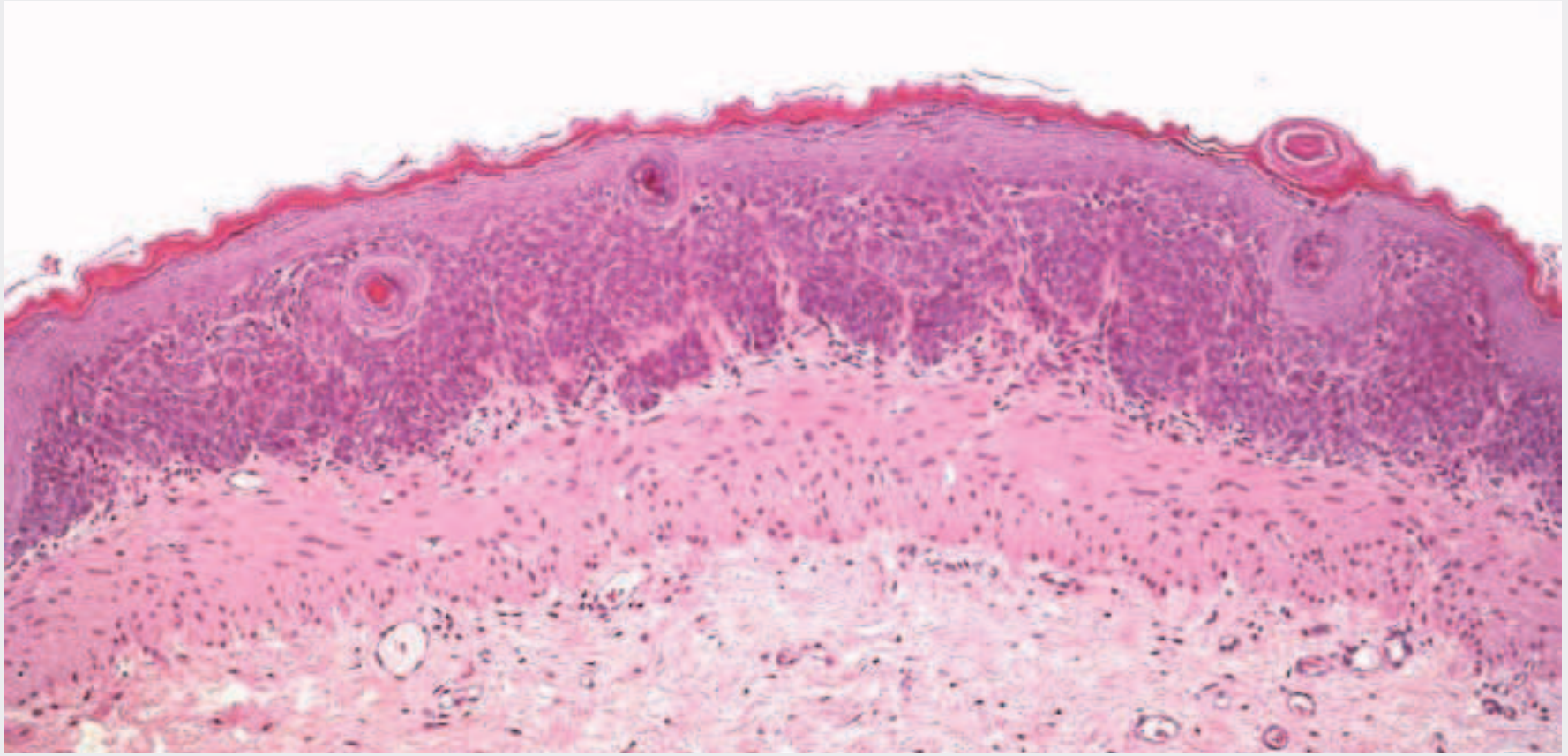
Hyperplaisa, basal cell (rat)



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Nonglandular stomach

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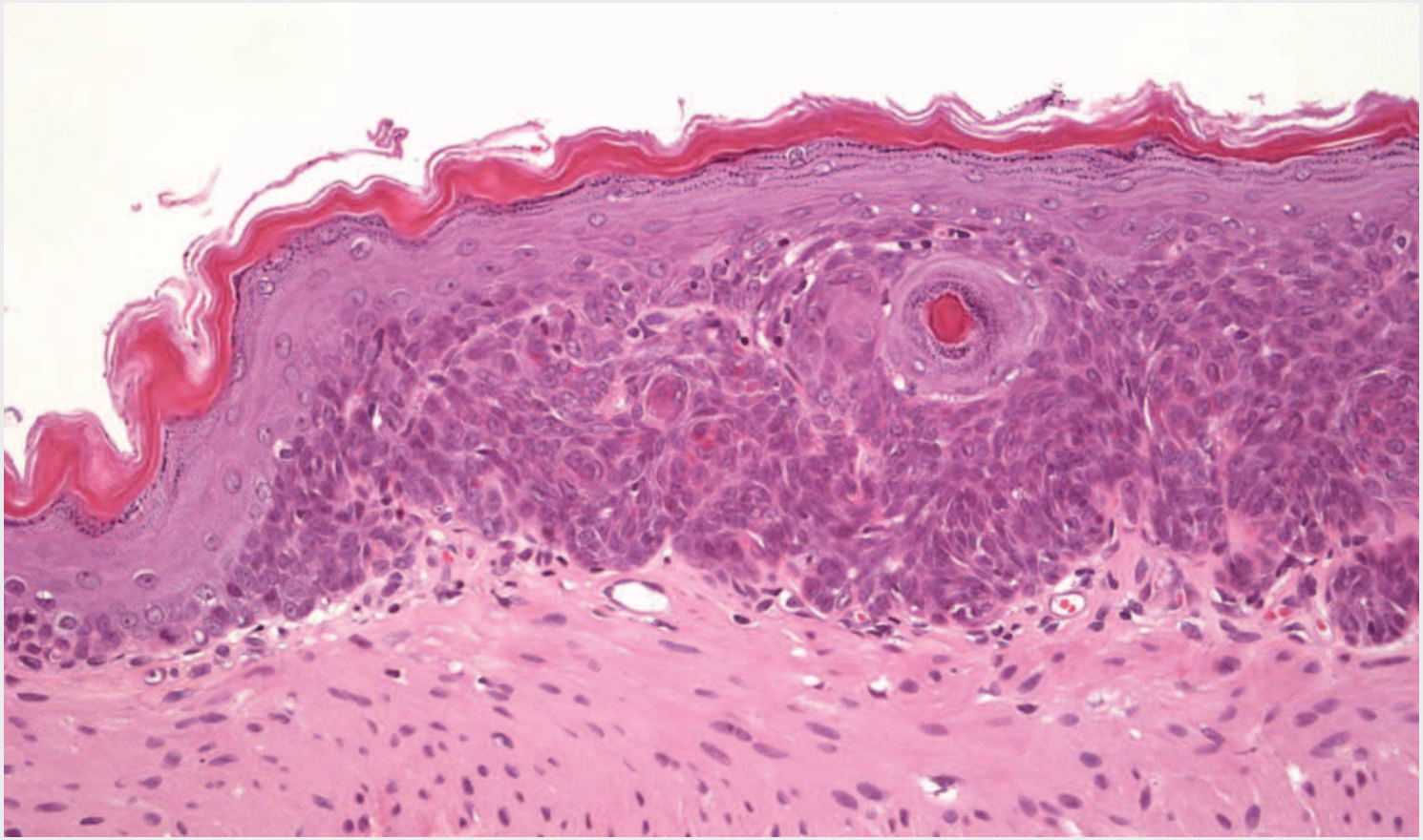
Hyperplaisa, basal cell (rat)



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Hyperplaisa, basal cell

Differential diagnoses

Hyperplasia, Squamous Cell:
Thickening of the epithelium with all normally existing layers.

Carcinoma, Squamous Cell:
Evidence for lost basement membrane integrity, spinous cells and keratinized cells proliferate, cellular atypia.

Tumor, Basal Cell, Benign:
Circumscribed proliferation of basal cells with loss of rete peg structure and leading to compression of surrounding tissue or prominent elevation of overlying epithelial layers.

Tumor, Basal Cell, Malignant:
Basal cells predominate, keratinization is missing, evidence for lost basement membrane integrity.

Nonglandular stomach

Hyperplaisa, basal cell

Specific cases:

Isolated nests of basal cells in the lamina propria

- With discrete borders indicating an intact basement membrane

→ Dependent on the plane of section through the rete peg structures

Foci of basal cell hyperplasia in the mucosa of the glandular stomach

- Always in the vinicity to the limiting ridge
- Morphologically similar to basal cell hyperplasia of the forestomach

→ Considered to originate from the forestomach

→ Should be recorded under “nonglandular stomach, hyperplasia, basal cell”.

Nonglandular stomach

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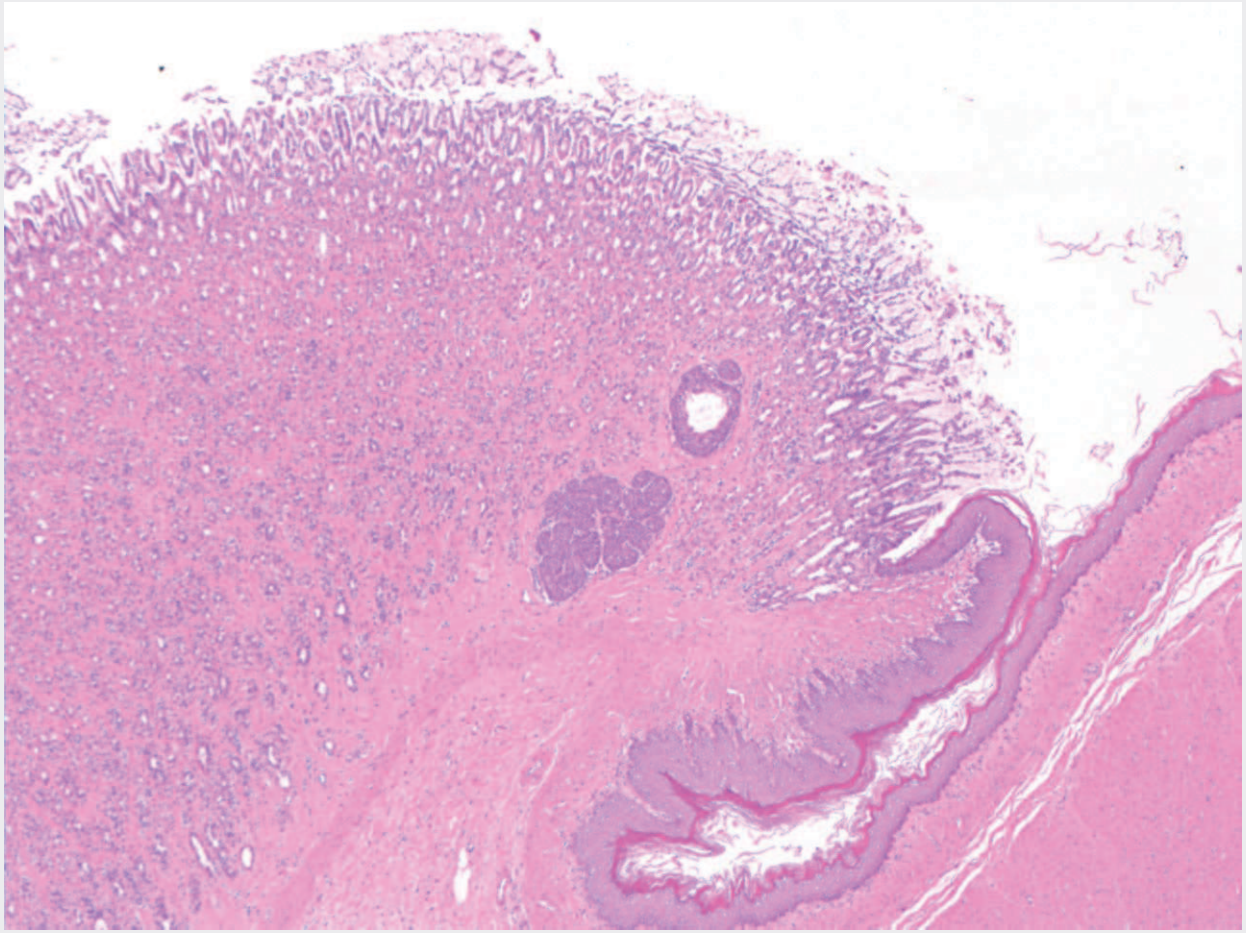
Hyperplaisa, basal cell



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Nonglandular stomach

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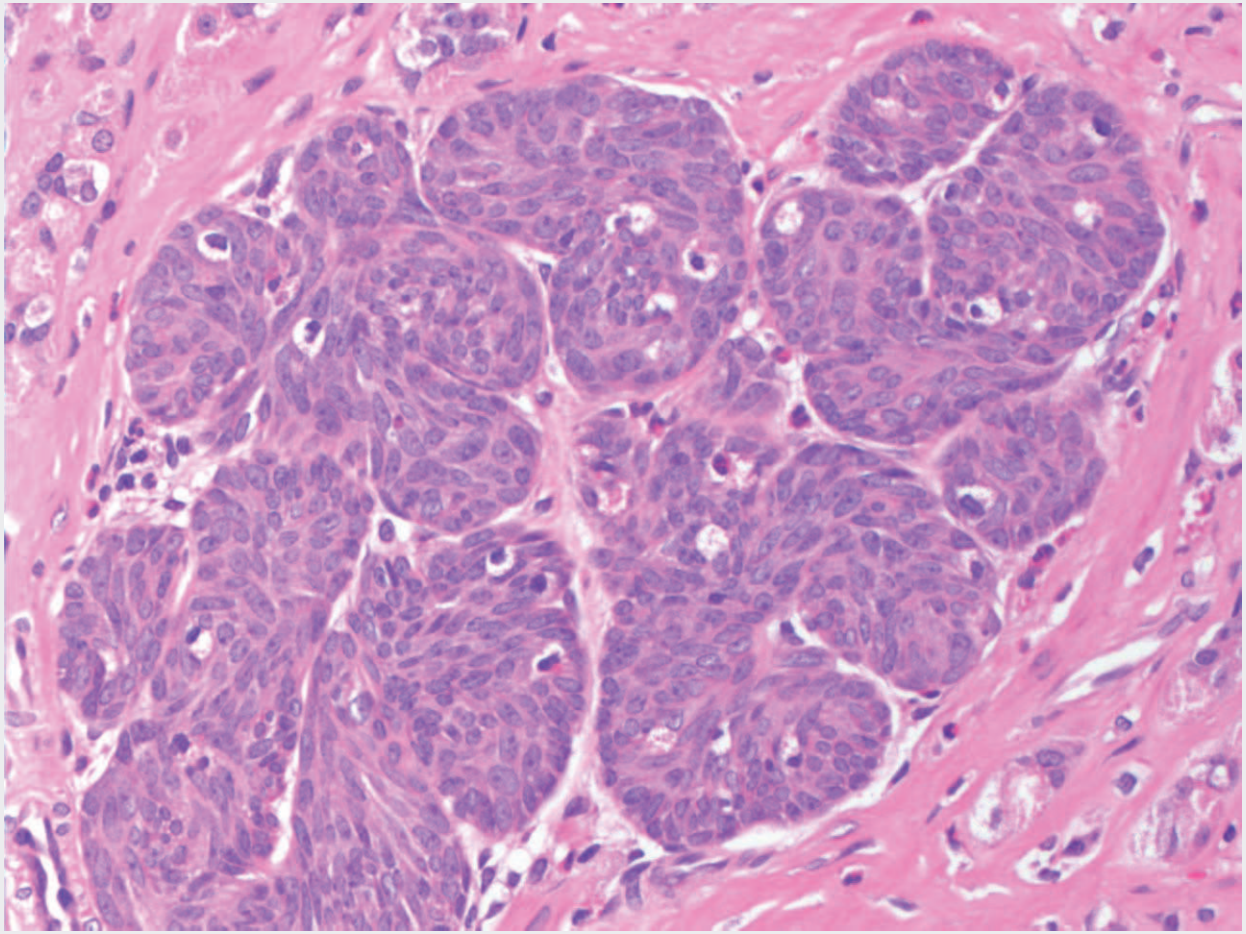
Hyperplaisa, basal cell



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Glandular stomach / intestine

Diverticulum

Synonyms: Cystic adenomatous hyperplasia; diverticulosis; herniated crypt; crypt herniation

Diverticulum, atypical, may have been identified as: Atypical cystic hyperplasia; cystic hyperplasia with growth into the gastric wall; cystic adenomatous hyperplasia; herniation atypical; “pseudoinvasion”, atypical; hamartoma, atypical

Modifiers: Cystic, atypical

Diagnostic features

- Extension of glands / crypts through muscularis mucosae, into submucosa and further in some cases.
- Morphology of epithelial lining is variable, ranging from single layer cuboidal or columnar cells to complete mucosa.
- Epithelium may show features of regeneration like increased basophilia, increased nucleus-to-cytoplasm ratio and gradual loss of polarity, but atypia is minimal at the most.
- **Basement membrane integrity is always maintained.**
- More often seen in the antrum and colon of mice.
- Often accompanied by inflammation and regenerative / reparative processes.
- May contain ingesta, hair, or other foreign material.

Glandular stomach

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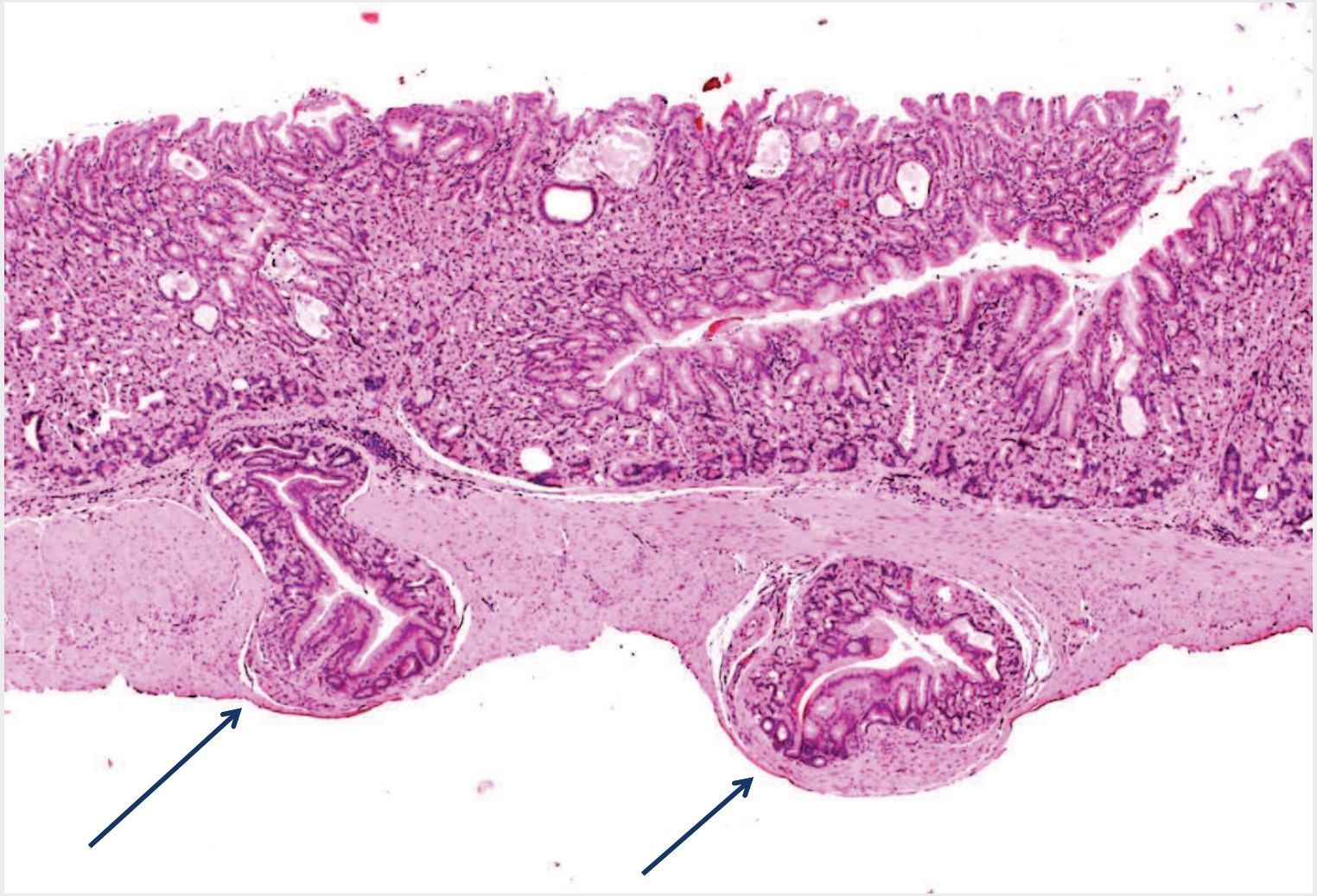
Diverticulum (mouse)



Glandular stomach

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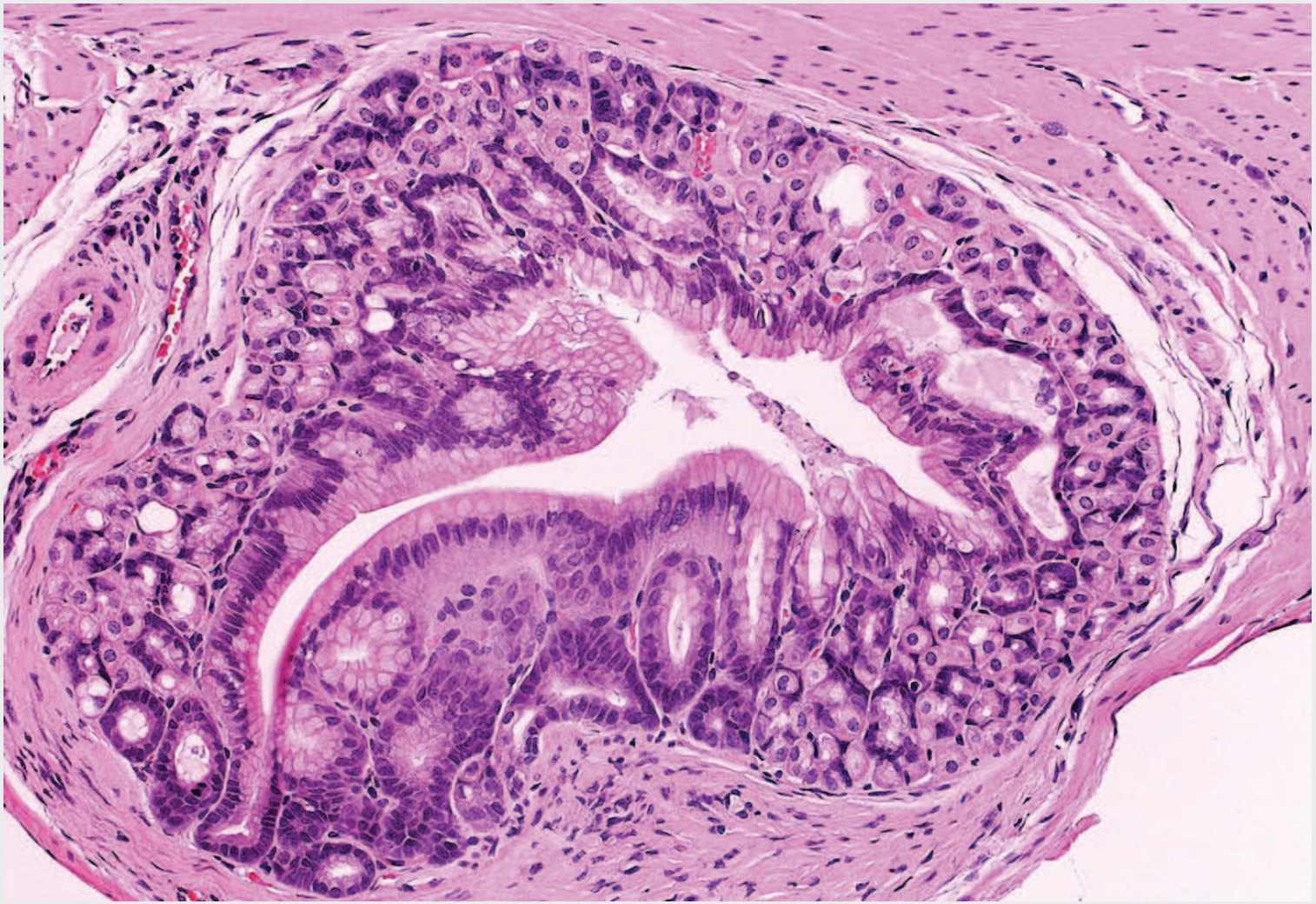
Diverticulum (mouse)



Intestine

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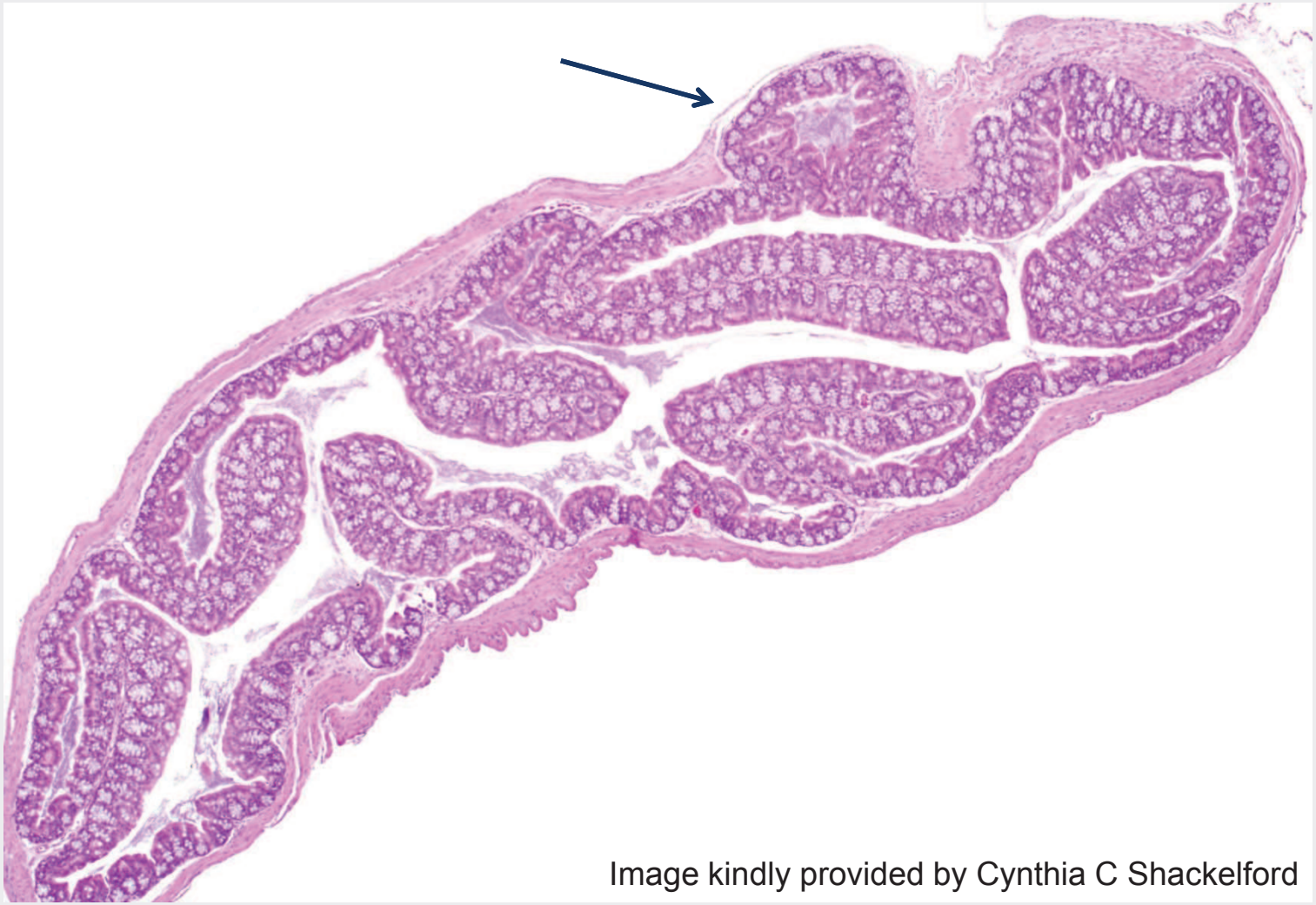
Diverticulum (mouse, colon)



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