5th Conference of STP-I

Spontaneous and induced lesions of the gastrointestinal tract

- INHAND nomenclature and diagnostic criteria (I) -

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INHAND: Some general aspects

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

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: Some general aspects

**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

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
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
Lesions to be presented

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

Hyperplasia, 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

Hyperplasia, basal cell (rat)

Image kindly provided by RITA
Nonglandular stomach

Hyperplasia, basal cell (rat)

Image kindly provided by RITA
Nonglandular stomach

Hyperplasia, 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

Hyperplasia, 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 vicinity 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

Hyperplasia, basal cell

Image kindly provided by RITA
Nonglandular stomach

Hyperplasia, basal cell

Image kindly provided by RITA
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

**Diverticulum (mouse)**
Glandular stomach

**Diverticulum (mouse)**

![Micrograph of Glandular stomach](image_url)
**Intestine**

**Diverticulum** (mouse, colon)

Image kindly provided by Cynthia C Shackelford