Importance of high quality data base systems in the study of genetic characteristics in horses

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Outline

❖ role of genetic defects and characteristics

➢ genetic background and examples (cattle, horse)

❖ role of data base systems: monitoring and interpretation

❖ Warmblood Fragile Foal Syndrome (WFFS) as a famous example

➢ disease characteristics

➢ statistical analyses: WFFS mutation and equine reproduction data

➢ distribution patterns

❖ conclusions

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Genetic background

❖ replication error during meiosis (parent → offspring)

  ➢ apparent in the next generation

  ➢ consequence could be: neutral, trait, disease or unknown

  ➢ often recessively inherited

❖ selection → increase of inbreeding

  ➢ stronger relevance of mutations

❖ extensive recording of phenotypes, ancestral and genomic information

  ➢ facilitating the discovery of mutations

Example: Cattle breeding

- ❖ since introduction of genomics
  - ➢ discovery of several deleterious genetic defects (BLAD, Brachyspina etc.)
  - ➢ as well as: single gene effects without any negative consequences (colour genotypes, polledness, casein etc.)

→ genetic <u>characteristics</u> instead of genetic defects

Genetic characteristics in horses

❖ routine screening in some horse breeds, e.g.:

➢ Arabians (SCID, CA, LFS etc.)

➢ Quarter Horses (PSSM, HERDA, HYPP etc.)

❖ in the past:
Warmblood breeders not so familiar with molecular genetic testing

❖ main point of contact with laboratory work:

➢ parentage testing

➢ testing for colour genotypes

Role of data base systems

❖ how to control, understand and discover genetic characteristics?

➢ informative and enough data

➢ stored and managed in one central location

❖ comprehensive data base system needed for:

➢ monitoring and interpretation of genetic characteristics

→ essential for a responsible handling by the breeding organizations

Warmblood Fragile Foal Syndrome (WFFS)

❖ <u>hereditary connective tissue disorder</u>
in Thoroughbred and Warmblood breeds

❖ first described in 2011 (US research group)

➢ commercial genetic test since 2013

❖ became widely known among breeders in 2018

➢ WFFS case in the USA → discussed internationally

→ WFFS as an example how to elucidate a genetic characteristic
with the help of a comprehensive data base system

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WFFS – disease characteristics

❖ point mutation in the PLOD1 gene, recessively inherited

❖ consequences of mutation:

➢ thin and fragile epidermis – not firmly attached to the subcutaneous tissue

➢ even low stress leads to skin rupture

➢ hyperextensible joints of the limbs

❖ only few affected (homozygous) foals are born → not viable

→ what about WFFS related losses?

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Monthoux et. al, 2015

a   b
Monthoux et. al, 2015
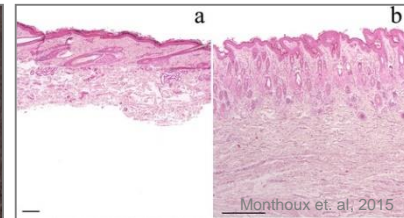
Hardy-Weinberg equilibrium (HWE)

biologyexams4u.com

$$p^2 + 2pq + q^2 = 1$$

❖ mathematical model from population genetics

➢ null hypothesis of relationship
between allele and genotype frequencies

❖ reported carrier (heterozygotes) frequency of 9.5-15 %

❖ mating a carrier sire to the average mare population

➢ estimated value of 2.4-3.7 % homozygous offspring (following HWE)
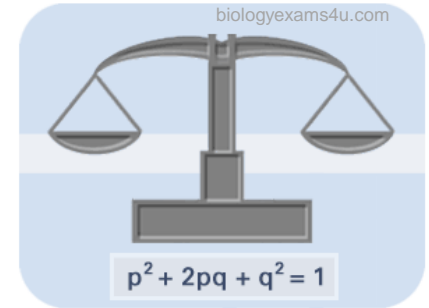
→ 2.4-3.7 % more foal losses (because of WFFS) expected

HWE – Explanation

probabilities of genotypes with random mating (11 % carrier freq.)

sire \ mare pop.	AA (89%)	Aa (11%)
AA (free)	all free (AA)	½ free (AA) ½ carrier (Aa)
Aa (carrier)	½ free (AA) ½ carrier (Aa)	¼ free (AA) ½ carrier (Aa) ¼ affected (aa)

0.25*0.11 = 0.028

expected: 2.8 % homozygous offspring (more foal losses)

Analyses with equine reproduction data

❖ covering data from 10 German Horse Breeding Associations

➤ N = 426,568 coverings of 10 years (2008-2017)

➤ N = 177,582 coverings from stallions with known WFFS status

❖ **analyses of variance** with SAS software (v. 9.2, PROC HPMIXED)

➤ dependent variable (1/0):
foal was born (1) or foal was not born / died within the first 2 days (0)

➤ fixed effects:
WFFS status of the sire, data provider, covering year, age of the mare

➤ random effect of the sire himself + random residual

Analysis of variance – Results

❖ expectation (following HWE):

➤ <u>2. 4-3.7 %</u> more foal losses among carriers than free sires

❖ results based on all sires with known WFFS status

➤ least square means of the foaling rates

dataset restriction	least square means foaling rates		difference free vs. carrier	p-value WFFS status
	carrier	free		
none (a)	0.6393	0.6636	0.0243	0.0304
min. 5 foals per sire (b)	0.6388	0.6638	0.0250	0.0264
min. 5 sire per provider (c)	0.6550	0.6783	0.0233	0.0397
combination of (b) and (c)	0.6552	0.6792	0.0240	0.0347

WFFS – Distribution patterns (I)

❖ WFFS known for several breeding populations
(cases in USA, SWE, CH, DK, GER)

  ➢ mutation must be rather old

  ➢ first occurrence in a founder who is an ancestor in many populations

  → English Thoroughbred was / is used in many different breeds

❖ data analyses: WFFS tested horses (N = 3576) and their ancestry

  → which founder appears in the pedigree of all known carriers?

WFFS – Distribution patterns (II)

www.horsemagazine.com

- ❖ only horses which appear in every known carrier
  - ➢ Dark Ronald xx, born 1905
  - ➢ his father Bay Ronald xx, born 1893
  - → very influential English Thoroughbred horses

- ❖ skeleton, heart + skin of Dark Ronald xx in a museum in Halle (GER)
  - ➢ sample from heart / skin was taken
  - ➢ DNA extraction and testing in progress
  - → spread of mutation i.a. via Dark Ronald xx and others

www.campus-halensis.de

- ❖ note: origin of the mutation most likely much older

Conclusions

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❖ inheritance theory confirmed by foaling rates

➤ WFFS as a cause of premature foal losses

❖ to avoid affected / stillborn foals and abortion: use the possibilities of modern breeding!

➤ WFFS can be controlled by targeted testing and mating

❖ one distribution path of the mutation could be found

→ not possible without the power of strong data base systems

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Thank you !

Take home: frequent mutations → technical advances help elucidating relevant genetic characteristics

→ growing importance of meaningful data collection, responsible data use and strong data base systems

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