Genetic Testing to Improve Canine Health: **The Big Picture**

Brenda N. Bonnett

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Learning Objectives:

- 1. Describe One Health aspects of genetic testing including impacts and limitations of comparative research, direct to consumer testing, and application to individual vs. population health.
- 2. Demonstrate the need to apply and interpret genetic testing information in the context of wider aspects of health, welfare and human-dog interactions.
- 3. Identify tools to support client communication and genetic counseling for practicing veterinarians.

Brenda N. Bonnett

- Veterinarian, theriogenologist
- Epidemiologist
- Former tenured faculty Ontario Veterinary College
- Research:
 - Population health; many species; breed-specific dog, cat, horse
 - Veterinary communication
 - Human-animal interactions
 - Pet overpopulation
 - Reproduction
- brenda.bonnett@ipfdogs.com



International Partnership for Dogs

IPFD – enhancing the health, wellbeing and welfare of dogs

- Multi-stakeholder
- International
- Sharing, collaborative
- Participatory

- Arms-length, independent Collective evidence and opinion Strength in numbers and diversity
- Tools and Resources

•





One Health recognizes that the health of people is connected to the health of animals and the environment. It is a *collaborative, multisectoral, and transdisciplinary approach—working at the local, regional, national, and global levels*—with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment.

One Health - It's all connected

One Health is the integrative effort of multiple disciplines working locally, nationally, and globally to attain optimal health for people, animals, and the environment. Together, the three make up the One Health triad, and the health of each is inextricably connected to the others in the triad. Understanding and addressing the health issues created at this intersection is the foundation for the concept of One Health.

What is One Health?

What can you do? What's the AVMA doing? How was the One Health Commission formed?

Additional Resources

Veterinary medicine is the only profession that routinely operates at the interface of these three components of One Health.

Efforts by just one sector cannot prevent or eliminate the problem.



These concepts apply **beyond infectious disease**... beyond zoonoses... beyond food safety ... One example:



[[add link]]





Benefits of a One Health approach **for genetic testing**?

- Many of the same issues affect animals and humans
 - Efforts by just one sector cannot prevent ... and in fact, may contribute to the challenges
 - Efforts by more than one sector are needed to address the issues.
- ISSUES??
 - Biologic, disease, etc.
 - But also: Impacting factors attitudes, societal, cultural...





Genetic testing....

General categories:

- Ancestry / Breed
- Identity/Forensics
 - **Public health** • Dog bites... dog poop
 - Tracking movement
- Disease / Clinical
- Breeding decisions

Applications and impacts:

- Individual
- Populations





PERSONALIZED MEDICINE --- the future!!

When it began...Tests were ordered through health practitioners – with pre- and post-test counselling. Now??

Direct To Consumer (DTC) Popularized thru Social Media Massive marketing push



Find out what your DNA says about your health, traits and ancestry.



https://www.23andme.com/?myg02=true



Health Predispositions* Learn how your genetics can influence y chances of developing certain health co

™ Atlantic



NOW WITH 1000+ REGION Ancestry Discover where your DI regions worldwide - and



Wellness Learn how your genes p being and lifestyle choi

SCIENCE

Popular

What Vets Think of '23andMe for Dogs'

Magazine v

More and more companies are selling DNA-test kits for pets.

Sections ~

SARAH ZHANG NOV 12, 2018

Latest



VITOONY35 / SHUTTERSTOCK

https://www.theatlantic.com/science/archive/2018/11/vets-dog-dna-test/575152/

Evolution of Genetic Testing??

Cutting-Edge Science

2005

1920's



SciFi



Figure 1. Tasha. Scientists sequenced the first canine genome using DNA from a boxer named Tasha.

And Now??

Cutting-Edge Science

Social Phenomenon

2005

1920's



SciFi



Figure 1. Tasha. Scientists sequenced the first canine genome using DNA from a boxer named Tasha.



How to Throw a **Dog Breed Reveal Party**

https://petcentral.chewy.com/how-to-throw-a-dog-breed-reveal-party/

Pages and pages of memes on ancestry and parentage DNA testing results



Google search

Emerging concerns....



ancestry-test-results-explained.html



More than 26 million people have taken an at-home ancestry test

The genetic genie is out of the bottle. And it's not going

back. https://www.technologyreview.com/s/612880/more-than-26-million-peoplehave-taken-an-at-home-ancestry-test/

Emerging concerns...

Weird acceptance/trust in DNA testing and those that are selling it??

Sk NEWS	POLITICS	U.S. NEWS	BUSINESS	WORLD	TECH & MEDIA	THINK	HEALTH	SPORTS	
AGING	Genetic off Medi	-test icare	ing s	can	n targe	ets	seni	ors and r	ips
	Capitalizing on the growing popularity of genetic testing, scammers are persuading seniors to hand over their DNA not knowing it may lead to identity theft and Medicare fraud								

https://www.nbcnews.com/health/aging/genetic-testing-scam-targets-seniors-rips-medicare-n1037186

One Health: Translational Medicine

- In the last 15 years (2010), the domestic dog has emerged as a powerful genetic tool for the study of heritable human diseases. Human disorders associated with immunodeficiency, narcolepsy, metabolic disease, cancer, autoimmune function, vision and epilepsy
- vision, sleep and immune function, have informed us about how to better understand the comparable human disease
- Cancer !

tor Dog

- Many (most?) with a similar condition in humans AND predominantly single gene disorders... Why?
- How do conditions with DNA tests compare to lists of common/important diseases in dogs? "easy" funding ternational



What disorders most commonly affect our dogs?

The study



The Aim - To identify the most common conditions affecting dogs in England.

The Data - Random samples taken from 148,741 dogs, attending 93 vet practices.

ngland.

(a)



Most common diagnoses Ear canal conditions 10.2% 0 **Dental disease** 9.3% 0 Anal sac impaction 7.1% 0 **Overgrown** nails 7.1% 0 Arthritis 6.6% 0 Diarrhoea 6.4% 0 Obesity 6.1% 5.5% 📕 Injuries

Top 10 Canine Health Concerns (AKC-Canine Health Foundation)

#1 Hip Dysplasia

#2 Allergies

#3 Epilepsy

#4 Hemangiosarcoma

#5 Hypothyroidism

#6 Lymphoma

#7 Patella Luxation

#8 Cataracts

#9 Bloat

#10 Atopic Dermatitis

Brachycephalics:

BOAS, Breathing problems, eyes, locomotor...

Genetic testing not available for most – most of these are 'complex' diseases!





Genetic Testing – why is it done?

- Individual animal
 - Breed background/ heritage
 - Diagnosis/ prognosis/ therapy
 - KCs/ Registries/ Forensics
 - Dog ID
 - Parentage

- Breeding
 - Risk reduction
 - Selection or avoidance of characteristics
- Breed/ population
 - Risk/ prevalence
 - Diversity

- Veterinarians
 - Clinical / individual
 - Diagnostic/ therapy
 - Marketing preventive medicine





Genetics and genomics – opportunities and challenges for veterinarians

- Overwhelming amount of information
- New new new
- More more more
- Public perception... don't just need to educate... you need to *de-educate* and try to change behaviours and beliefs





Ancestry – opportunities and challenges for veterinarians

- Understanding and misunderstanding
- Breed-reveal parties??
- Purebred dogs???
- Exaggerated claims on breed impact
 - Evidence??? E.g. breed differences nutrition? Behavior?







"Personalized medicine" – opportunities and challenges for veterinarians

- Everything you need to know about health can be provided by a DNA panel – dangerous misconception
- Marketing focussed on number of tests offered...
 - Breed relevance???
 - To varying extent leaving it to the consumer to figure out the results, *"results may not apply in your breed"*
- Technology has outpaced our knowledge about how to interpret and apply it. Perhaps not accounted for the human factor...





When DTC testing goes wrong... sometimes with the help of health care professionals

HUFFPOST PERSONAL

Got A Double Mastectomy After A Genetic Test. Then I Learned The Results Were Wrong.

https://www.huffpost.com/entry/brca-genetic-testingmastectomy_n_5c6c39fbe4b012225acd80d3

The "Angelina Jolie" Effect

A spike in genetic tests for breast cancer after actress' public disclosure, but no corresponding increase in mastectomies

https://hms.harvard.edu/news/angelina-jolie-effect

Breeding decisions –

... I used to say that this aspect was mostly just an issue on the veterinary side...







One of the most important causes of genetic disorders in newborns is <u>consanguineous</u> <u>marriages</u> - highest in Zanjan Province at 49.6%

Penale ③ Falmulary 10, 2017 17:53

Premarital Genetic Testing Mandatory

One of the most important causes of genetic disorders in newborns is consanguineous marriages. Currently, the rate of marriage within families is 12.6% in Iran, with the highest in Zanjan Province at 49.6% Every day, 80 infants with some form of disability are born in the country. That equals to over 30,000 new disabilities per year.



LIVE TV Edit

Inside Africa

In Nigeria, your genetic makeup can decide if you get a second date

By Aisha Salaudeen, CNN (3) Updated 1:01 PM ET, Wed July 10, 2019

https://www.cnn.com/2019/07/10/health/genotype-dating-nigeriaintl/index.html



In May, the Anambra state parliament in Nigeria's eastern region passed a bill making genotype testing compulsory before marriage.

Pheramor | Using Science to Find Love

<u>Pheramor</u>, a Houston-based online dating startup that claims to **use your DNA as** the secret sauce in its matchmaking formulation.

... <u>23andMe</u> meets <u>Tinder</u> meets monogamists.

https://www.pheramor.com/

Of course, **sexual chemistry** isn't just about <u>deoxyribonucleic acid</u>. And so

https://www.genepartner.com/

in addition to the 11 "attraction genes" Pheramoruses to suss out biological compatibility, the company als social media profiles, to be da



Love is no coincidence!

Matching people by analyzing their DNA



Order a GenePartner Test

Dating Sites & Matchmakers



There is currently no quality control system for DNA testing in veterinary medicine

no standards... no rules or regulations about who can offer tests, etc. etc.





Harmonization of Genetic Testing for Dogs

Are you yelling Help!! ... ???

Help is on the way...

International Partnership for Dogs



Do DNA Tests Work? Pet genomics medicine runs wild \$ Big Business € HOT TOPIC Interest of the second seco **Dogs: Balancing daunting** challenges and great potential https://dogwellnet.com/content/health-and-breeding/screening-tests/dna/dna-tests-for-use-in-breedingdecisions/genetics-and-genomics-for-dogs-balancing-daunting-challenges-and-great-potential-r597/

5 years ago – 2 years ago – now - future

- Too many new DNA testing labs.... Maybe too few IPFD Harmonization of Genetic Testing for Dogs HGTD
- Rapid commercialization......

https://dogwellnet.com/ctp/

- All tests on All Breeds
- Validation from discovery to application even more of a problem
 - Publication delays... or?
- Big Picture of health and disease being lost??

COMING SOON:IPFD/IDHW Validation Matrix for Genetic TestingIPFD Expert PanelIPFD Health Strategies Database for Dogs

DogWellNet

International Collaboration For Dog Health And Welfare. Join Us.

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 DogWellNet
 Harmonization of Genetic Testing for Dogs
 HGTD GOAL: Improve standardization of, and access to, robust genetic testing to support health improvements and a sustainable future for healthy dogs. *The* portal for information on Genetic Testing Providers (labs); genetic tests, and tests by breed. There are two major components: the Quality Testing Database and Genetic Counselling resources.

IPFD cannot be held responsible for inaccurate content or any outcome from the use of information or resources found on this site.

More >>

HGTD Database Resources

Search.

Ann Milligan *

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How to use the HGTD HGTD Quality Indicators Acronyms - Mode of Inheritance

FAQs

Accreditation Basics

This brief overview may help you identify what types of accreditation are important to you, when choosing your genetic test provider.

Accreditation and Industry Standards

List of organizations throughout the world that are involved in matters of accreditation and establishing industry standards.

Choosing a Genetic Test Provider

HGTD - Quality Testing Database





https://dogwellnet.com/ctp/

HGTD Quick Search

Breed Test/Disease Lab/GTP

+ Create - 🔊 Activity Streams - 💄 🔤

Contributing Leadership Sponsors



Quick change from resistance to

- overemphasis on DNA tests over all other health evaluations.
- 'early adoption of tests without adequate validation for specific breed/disease situation
- *Misunderstanding* of proper application of test results
- Decision-making by facebook.



Hesitance of Kennel Clubs to STOP breed clubs from implementing health testing??

French Bulldogs (FBDs) and Degenerative Myelopathy (DM)

- Testing and recording of results in several countries
- Testing implemented based on 'allele frequencies' i.e. test results possibly without consideration of actual occurrence of DM in this breed.
- E.g. data from French Kennel Club (SCC):
- NOTE!! These are allele frequencies results of tests not estimates of disease.

Although the SCC uses 'carrier' and 'at risk' many reports use 'AFFECTED'. They may mean 'genetically affected' but many consumers interpret this as meaning the dog has the disease... or will have. Results for French Bulldog
25/06/2019DM1A-1.1 (clear)324DM1A-1.2 (carrier)145DM1A-2.2 (at risk)8

Degenerative Myelopathy (DM)Has never been confirmed to occur inFrench Bulldogs... Dr. Jerold BellLINK:
Degenerative Myelopathy (DM) in French Bulldogs

So ... there seems to be a testing program for a disease that does not exist in this breed. Dogs may already have been removed from breeding because of test results. Is there an even bigger danger??? DM genetic variant has been accepted to be 'causative' in several breeds, e.g. German Shepherd.

How can Frenchies have the gene but not the disease:

- 1. The gene is not causative in this breed, or
- 2. Dogs that carry the gene have other genes that prevent that gene from being expressed.

We know there are modifying genes for various conditions... and it is not impossible that there are genes or groups of genes that can theoretically provide extra resistance to an individual, e.g. theoretically to one or more similar diseases.

IF this were the case —we would NOT want to remove those individuals from the breeding population? Something to consider.



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DISC/VERTEBRAL





TheseDNA tests are available, but do they help with the **most important concerns in the French Bulldog**?

- Chondrodysplasia
- Cystinuria Type I-A
- Degenerative Myelopathy
- Congenital Hypothyroidism
- Hyperuricosuria and Hyperuricemia (HUU)
- Canine Multifocal Retinopathy 1 (cmr1)
- Primary Hereditary Cataract (PHC)
- Progressive Retinal Atrophy cord1
- Coat Colour Dilution, Alopecia

How does it happen that a test becomes required or widely used when it doesn't reflect the actual disease status in the breed?

- Attitudes that DNA is always right
- Panel testing and blanket reporting of results, including those that are not validated/ not 'breed-relevant' that cause concern in the owners/breeders.
- Lack of information on prevalence- of disease... i.e. genetic information but poor information on phenotypes; perhaps very very rare or unrecognized.

DM listed as available in the HGTD:
Number of breeds for which the test is offered?
173 ... Maybe as few as 30 *fully* 'validated'???

The cautions we should take-away include:

- Just because a disease has been studied and a test has been developed does not mean it is an important disease for the breed or the dog population in general.
- Every dog and every human has mutations!!

There will always be an increasing number of inherited diseases discovered. We must learn to balance evidence on importance, application, validity etc. to appropriately take advantage of the tremendous potential for advanced technologies to inform our practice while not being misled by spurious results. We must increase availability of counseling and appropriate interpretation of genetic tests – maybe we have to proactively try to counteract the forces of commercial

marketing and the media!

Widespread DTC Genetic Testing

• Can we be sure that GT do more good than harm from the individual

to the population level?

- What are the risks and benefits and how do we manage them?
 - for the 'Big Picture of Health'
 - And for populations e.g. impact on genetic diversity



Take home these nuggets

- From discovery through commercialization to application with DTC marketing thrown in the mix – from the individual to the population – work in dogs is informing human genetics and genomics and people interacting with genetic testing is impacting dogs
- Human attitudes and behaviors may have a faster and stronger impact than science... in how the world of genetic testing evolves
- Future One Health aspects may be even stronger as we move into epigenetics and complex diseases and examine environmental influences.





Benefits of a One Health approach for genetic testing?

- Many of the same issues affect animals and humans
 - Trends are reflected across human and pet genetic testing
 - Attitudes, beliefs and trends are driving use of genetic testing as much or more than science.
 - Tools are and will increasingly be available to support veterinarians to take a balanced and big picture role.
 - Need for proactive education to counter marketing forces??
 - Or, get on the band wagon?



