

## HOW RESEARCH WORKS

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*(This first appeared on a Great Dane list a few years back. The author has given permission for BeaCon to reproduce the article in our newsletter. We believe this article will help Beardie folks better understand what transpires as BeaCon begins work to identify and bring new health problems to the point of research. One topic we have discussed is symmetrical lupoid onychodystrophy [SLO] about which more will come in the future. E Sell)*

There always seems to be a lot of confusion about how scientific research works, so I thought I'd write a little outline that might help. Research is a confusing topic as it's outside the experience of most people & functions by rules and restrictions unfamiliar to most us normal folks.

So hopefully this will help understanding, which can reduce the frustration people often have about research in that they have false expectations of what to expect, given they are unfamiliar with how things simply have to work when, for example, trying to track down the genes behind some canine disease. This is just an outline, written in broadstrokes and is to be taken that way, not as a detailed explanation of all or any particular research work.

Research isn't just a matter of finding an able party (i.e. a scientist), nor is it just about funding, for all these are needed. Research, from the researcher's perspective, has to be productive to be of interest. So not only does the research project have to dovetail with the scientist's abilities, facilities and background, s/he is going to have to feel there is a fair chance to be able to recruit and assemble the target population, that the problem can be solved with the tools to hand, and there has to be no better project offered for the same limited resources of time, personnel, lab resources, and money.

Typically, with veterinary research, the work can really depend on what walks through the door (especially when it comes to dogs); they have to know they are going to have the subjects they need to actual make progress. There are other ways to recruit a target population (more on that in a minute), but each project has constraints that mean

all styles won't always work, and this HAS to be assured before a project can actually become research.

Research therefore usually starts with a target case: some individual or set of individuals with what seems to be a shared problem that science already knows something about. At this point this isn't really more than a tentative project. If the researcher can develop some leads as to what kind of analysis the problem might lend itself to, then they can see if they have the needed tools to do the work, if they can develop the background to get support, if they can find enough individuals with the common problem, and then they have just begun--we are not really even yet to the point of \*having\* research, just to the point of being able to (maybe) start a research project. Grants are only given to those scientists who can demonstrate they have the tools, skills, ability, people & materials needed, and who can demonstrate, using the work of other scientists, that there is good reason to believe their hypothesis and so to support their research. All this to just get off the ground.

Once research has actually started, for example, when the CHF reviews a grant a scientist has submitted and suggests to the relevant breeds that they consider supporting this research, then we are at the first stage. (Often this really takes some time & effort, and many attempts at the preliminary level don't turn out, so don't turn into research. So people in the preliminary stage can feel very frustrated.) This is the point where a certain population is recruited to gather together candidates for the initial group. This group has to be EXACT; it has to have particular traits & has to commit to supplying particular samples, sometimes over a long period of time, sometimes involving many exams.

There is always the chance a group or an individual, at any phase of the project, is not going to fit the needed data, and so will be rejected. This isn't personal, but research, to be considered quality, has to be exact. Anytime there is a question if a dog or a family doesn't fit the research parameters, they have to be turned away, as otherwise the results of the research will be considered contaminated, and all of it will be seen as dubious and so is wasted. You cannot start with "muddy water" if you plan to later claim you KNOW something and can prove it. In

fact at each phase you have to keep your data pristine so it's seen as valid.

We often today talk of "having researched the breed," and/or talk of doing online "research," so we tend to think it's just a matter of looking things up, asking questions and so on. Scientific research isn't like this. It's more like detective work and often you don't even know what questions to ask and often you get answers you never expected. And, for all it may not be fair, some of real health issues are also the harder problems and so are not going to be chosen, as science is all about asking questions and trying then to find the solutions to them. A question can be *very* important and still be far too mysterious at this point in time for science to tackle.

If the tools are not there and/or if success isn't likely, no researcher is going to reasonably be able to work on it. They need to be in a learning curve themselves, that's what being a scientist is all about, the excitement of learning, of "cracking the code." SO they need to feel they are doing some productive work for personal satisfaction as well as to keep their jobs, their status and the respect of their peers. And feed their families.

And there are special constraints on research into pet species. For one thing, human research will naturally always be a priority for most researchers; secondly, when it comes to animal research, a lot of emphasis is going to be on commercial large animal studies (they are better organized and pay better, animals are easier to track and keep), and thirdly much research is going to want to use animal models to explore disease, and that doesn't always allow us the comfort zone of ethics we want as to how our dogs are going to be managed and treated. We are not typically going to donate large numbers of dogs from a family with a problem to live out their lives in kennels at some university, nor are we going to want to see potentially dangerous or uncomfortable procedures done on our beloved pets for the sake of learning as a rule.

Plus we do not, as a rule, have the sort of organizations in place to help researchers find the target population they need, we don't have a tradition of support, or even a tradition (as to horse and cattle people) of working with universities and researchers. Here we are just beginning where the cattle industry, for example, is miles ahead in being

able to promote and support research. So they get the researcher's attention, as the researchers feel confident about their involvement. They have a track record. And lots of problems can be studied in several species, so from the researcher's perspective, this matters.

So for all these general, as well as particular reasons, research is a somewhat difficult and challenging prospect for our canine and feline friends. Research takes years, decades: each phase in fact typically takes years, and at each phase there is a chance the research will be abandoned as not fruitful. More goes wrong in science than right, in the sense you simply must follow where the facts lead you, and be honest when they lead you nowhere. And that happens. And then you have to start over, rethink, find a new project, a new method of analysis, or something.

So no honest scientist (and they should be this above all else, as they need be ruled by clarity of mind) can say what tomorrow will bring and they tend to speak, especially to those hopeful, in somewhat cautious, even pessimistic tones. And we in the general population anyway don't often "speak the same language" as they do: scientists are immersed in their specialty and are more accustomed to talking to each other than to "us." Plus they are mostly very busy, and they generally do not anticipate having to talk to individuals who may feel they have a stake in the outcome of the research. Generally, in fact, it's expected they will simply write reports on a regular basis to the organizations they feel they need to account for the progress of their research with. It's unusual for any researcher to be expected to actually deal directly with the study's participants, so, for all that feels normal to us, it's not the normal thing for them. So we miscommunicate a lot.

Plus the exact research we want is what matters to us: we want this problem in that breed studied. But being able to hope for progress is what matters to researchers. As one told me recently, they do not like to write reports that say "no progress," and so don't want to take on projects that don't look to be fruitful (for whatever reason). Scientists are not dedicated to one breed like many of us are, and their connection to our breed is through how interesting to them our problems are. Interesting to a scientist means it's a fruitful problem, one they have some

reason to think they can have some success with if they choose it. And they typically have many choices on what to work on. And they go where the research leads them.

So we can help them pick us in several ways. We can be "savvy" about how it all works and not have unreasonable expectations. We can accept how it works, understand it's not personal when we (our dogs) are not needed or are rejected for a study. We can be patient, knowing the scientist is playing a very hard game of "Clue" and one that has a lot of false starts and often no solution, or takes you places you didn't expect, gives you results you never anticipated, and the only thing they can control sometimes is the data they put in, so they focus on it being "clean", but that doesn't mean they don't understand we are still upset when our dogs are sick, it's just that they cannot always help us--on any level, and that's a blunt fact.

But we can work together to help make our problems work for them, be approachable. For example, we can take a page from large animal folks, and have a focused force to interface for us with the science community (this is why the CHF is so important and representatives from various dog organizations need to step forward to act as liaisons mean so much). We can also not expect them to have time to talk to each of us individually or help with our individual dogs.

For all we would like these experts to have time for us they don't usually--not if they are going to focus on research. (We can use a clinician, our vet, or a referral for this individual attention.) We can hope for good progress reports, but know they will only come once a year or less often, not call, but wait for the liaisons to put out what the researchers send (and so look to the CHF website, for example, for results, not call the university). And we have to also realize with all good intentions of all parties, things are not typically going to go just as planned and sometimes we all are going to start over, let a project sit while new tools or ideas are made, or just be patient when it goes in a new, unexpected direction. That's just part of the gamble we have to take to get any progress at all.

I know this is already too long and still I don't feel I've scratched the surface. But I would like to give

one example that is recent from the Dane community.

A few years back I was getting a lot of calls from people wanting information on Addison's disease in Danes. Now this isn't "supposed" to be a Dane disease, it's "supposed" to happen typically in middle-aged females, and it's "supposed" to be rare in dogs and usually restricted to certain breeds (like Poodles). But I was getting a lot of calls on all Danes, young and old, female and male, and some were not just asking for help treating their dogs, but where was the research going as to this problem. So I went to the scientific community, found out who to ask, and asked this. And I was told this isn't a problem in Danes.....you get the picture. So I told them: "But I have all these Danes....." and they answered it was anecdote, a self-selected sample...which all came down to I was seeing something really not there as to research possibilities. And they had reason to think that, to be fair; everyone thought this wasn't in this breed except the people who had to deal with it directly.

So to make a long 3 year journey short - I kept asking around the research community, followed the work in other breeds, talked to the Health and Welfare liaisons in other breeds, to the veterinary community, while the people with the Addison's Danes kept pushing, and I finally got someone in research who was pretty far along in the research (on the third phase essentially, so a ton of work already done & a lot known, so might help us) to say they'd look at what I had. And when they did, they told me it wasn't enough.

And so they still were not interested--they said it would take them years to get enough Danes, and they could meanwhile work on other breeds. So I asked them what they had to had to take us seriously; they told me and I spent nearly a year assembling the dogs they needed. (I had help from some folks with Addison's dogs thank goodness, but I also had to go out and canvas the veterinary community, get the message out in veterinary journals, personally called a bunch of endocrinologists, write letters to vets, take calls day and night, assemble all the individuals and their information in format, etc.)

And then I gave the data to the researcher (who was really great to even TAKE data from me, something

they hadn't themselves assembled). And then they said: "Okay, we'll add Danes in, using this list." And THEN we had to go to the CHF to get permission to change the grant, and they wouldn't do that until the GDCA would promise the needed funds to support Danes being added (which the Board did, and fast, as we had a deadline or miss out on this phase, have to wait several more years). So now we are started. It took almost 5 years to get here. (And this was a fast and really successful venture.) And we don't know anything yet! The research itself is just started. It will be years before we have answers. If we are lucky it will be years...instead of decades ...or never.

That's just the way it works in research, it's a lot of cautious footwork, a lot of "dotting i's" and so on, a lot of false starts, disappointing results, **and to help them help us we need to understand what "rocks their world" as it were.**

1. They need a "good" project that can realistically be seen to be solvable.
2. They need assurance the group wanting it will provide the subjects and stay the course.
3. They need to be left to do their work once it's started.
4. They need our patience and understanding most of all. We find them frustrating at times, but I'm pretty sure the feeling is mutual.
5. One of the biggest problems in the dog community having research work for them is that we just don't have realistic expectations as we don't understand the constraints that scientists labor under.

So the better we understand them, the better we can get them to work for us! And, to me, that's the point, getting to know more about how disease works, finding better treatments & finding better ways to test for disease.