

# Why I Remain Unconvinced About Backcrossing

## Part One

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I absolutely believe in the *theory* of backcross! Contrary to false but understandable rumors, I am not prejudiced against it nor do I have a personal vendetta against those campaigning as supporters of it. My opinions would be unchanged whomever was responsible for its resurrection.

I am however engrained with professional rules of medical research, resulting from 10 years in the Clinical Investigation Division of the drug company discovering prednisone. Then, medical horrors occurred such as thalidomide producing deformed infants missing arms and legs despite plausible clinical data permitting its governmental release for prescriptions. Rivaling the Watergate hearings, the Kefauver Congressional investigation of the drug industry took place with blazing headlines. It resulted in rewriting laws governing FDA drug approval especially evaluating scientific data and credibility of results. "Schooled in fire" by those volcanic days, I now do my best to objectively evaluate scientific credibility with parameters like:

- ✓ Are the total number of patients sufficient?
- ✓ Is methodology of the study's research protocol complete, thorough and current for its goals of results and conclusions?
- ✓ Are those results and conclusions indeed reasonably credible based on the amount of data and the methodology by which they necessarily were obtained?
- ✓ How prestigious and how many medical journals accepting the research (and subsequently updated reports) in terms of the journals' reputation of peer-reviewing manuscript credibility before publication acceptance? Have the journals passed stringent accreditation by the U.S. National Library of Medicine?

I also turn to nationally-recognized experts for peer review of whatever disease is researched. Given the years during which all their professional days are exclusively filled with one subject, I reconcile their authoritative dictums with the research I am evaluating.

Total Number of Backcrossed Dalmatians?

Medical Profile of Published Backcross Articles?

With great anticipation, I went to the online backcross website expecting years of totaled clinical data and objective statements. Instead, with much disappointment, I found of all reports cited there for medical proof, **not one** had been published by an accredited peer-reviewed medical publication. All (excluding the experimental genetic test's) were from non-medical magazines. They also were old

and probably outdated, like a 26-year-old 1981 *AKC Gazette* article or a 17-year-old 1990 *Dalmatian Quarterly*. One, surprisingly not on the website, is a medical peer-reviewed article published 21 years ago in a 1986 veterinary journal. Perhaps it is not on the website because it was not a medical presentation of formalized clinical evidence supporting backcrossing. Instead, it was anecdotes reviewing the theory's history, not a research report with tabulated data. (A 1999 subsequent edition did not include anything about the backcross project as published 13 years earlier.)

In comparison, traditional requirements of research reports presented with organized scientific data saturate innumerable vet journal publications by the three stone specialists, Carl Osborne, DVM, PhD (the most famous worldwide expert), Joseph Bartges, DVM, PhD (the worldwide expert in Dalmatian Stone Disease) and Jodi Westropp, DVM, PhD. Dr. Osborne's most recent Dalmatian article was in late 2005, peer-reviewed and published by the top vet-accredited *Journal of the American Veterinary Medicine Association*. His impressive data were clinical evidence from almost 20,000 Dalmatians! The article coincidentally impacted on backcross methodology with Dr. Osborne's statement, "*... for as yet unidentified reasons, not all hyperuricemic Dalmatians [those with abnormally high uric acid in their urine] form uroliths [become urate stone formers].*"

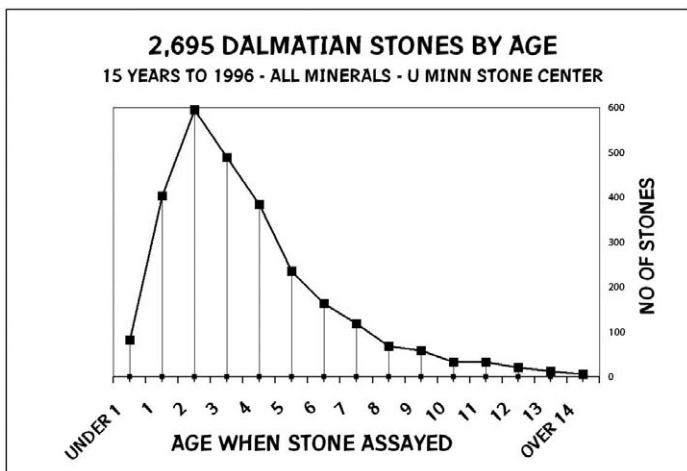
Dr. Osborne's statement lessening the significance of uric acid was startling coming from such a worldwide expert in a published article reporting on thousands of Dalmatians! In 2006, Dr. Bartges reinforced the impact on the backcross methodology with, "*All Dalmatians excrete 'increased amounts of uric acid' relative to other breeds of dogs, yet...[Dalmatian urate] stone formation is nowhere close to 100%...*" (Translation = Not every Dalmatian develops active urate stone disease despite all carrying the defect one manifestation of which is abnormal levels of urinary uric acid.)

These two experts' statements are the latest to discourage me. They intensified my discomfort about limited data presented solely for urinary uric acid throughout the years of backcrossings. My discomfort also originates from apparently few if any adults – only puppies – are cited as having been routinely tested for uric acid.

Because the stone experts, Drs. Osborne and Bartges, currently state abnormal uric acid is not the predominate all-embracing symptom of the Dalmatian defect, I now wonder if some backcrossed adults nonetheless develop active urate stone disease despite testing as low-uric-acid pups? It was revealed in January 2007 by the owner of the backcross project's website that the few dogs kept from the low-to-low breedings turned out to be carriers of the defect (heterozygous normal/low). The acknowledged existence of those adult backcrossed dogs seems to me to now require the withdrawal or rewording of the online generalization, "*...[the backcrossed breedline] produces the only Dalmatians in the world today*"

*that are free of a metabolic defect that can lead to urinary tract problems.”*

One graph in my 2006 Specialty lecture showed ages of 2,700 stone-forming Dalmatians reported by Dr. Osborne’s Minnesota Stone Center as ranging from pups to 14 years. Stone disease had its peak onset in those 2,700 Dalmatians between one and six years, the greatest number between two and three years of age. So, one immediately apparent backcross unknown is how many adult Dalmatians did or did not develop active stone disease at ages incriminated by Dr. Osborne’s Minnesota Stone Center for onset of active stone disease in thousands of non-backcrossed Dalmatians?



How dependable and predictive is puppy-only testing when those pups become adults living adult lives?

First reading about backcrossing years ago, I wondered why stone experts like Drs. Osborne or Bartges have never been called upon to contribute similar clinical knowledge into planning research protocols of the backcross theory. That still has not taken place to my dismay. Now that DCA has voted to open at least information dialogue such as this issue of the *Spotter*, I sincerely hope the influence of geneticists – valuable but limited compared to stone experts – will be soon balanced with urolithiasis specialists.

Another example of why? Dr. Osborne just informed me, as I write this article, the Minnesota Urinary Stone Center to date has reached data on over 310,000 stone-forming dogs! If since 1976 and after thousands of Dalmatian urinary stones, Dr. Osborne recently chose to publish, “... *for as yet unidentified reasons, not all hyperuricemic Dalmatians form uroliths*” it seems to me his expert’s statement underlines the need to reexamine research protocols in the light of today’s stone disease knowledge in order to confirm or deny the backcross theory. DCA recommendations should correspondingly also be deferred until updated, more credible medical evidence becomes available pro or con for backcrossed Dalmatians.

Let me end Part I by asserting I have not abandoned my hope for backcross. The theory continues with undiminished promise. But at this time, I do not find enough convincing evidence to dislodge my inability to accept its secular data and limited methodology. I am enticed by the theory but still not seduced.