

SPECIAL ARTICLE

The Cold, Hard Truth About Pediatric Research

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Over the past year I have had more than the usual number of opportunities to contemplate the status of pediatric research. I'd like to share with you what I believe is the cold, hard truth about pediatric research currently, and how the SPR and its members can respond to it. In considering this issue, I have discovered that in many ways, life in pediatric research today is much like life on the continent of Antarctica, and I will discuss the parallels with you.

Let us first consider the terrain. On Antarctica and in pediatric research the conditions can be harsh. Antarctica has the distinction of being the coldest, windiest, highest, and driest continent. Actual temperatures can be as low as -140°F . Importantly, resources are incredibly scarce on Antarctica. The statistics for land use provide a snapshot of the scarcity of resources: arable land in Antarctica, 0%; permanent crops, 0%; meadows and pastures, 0%; forest and woodlands, 0%; and irrigated land, 0%. In contrast, the "other" category comprises 100% of land use, but regrettably it is ice at 98% and barren rock at 2%. In pediatric research we are also currently dealing with a dramatic scarcity of resources, and single-digit percentages are a fact of present day life, particularly related to the budget crisis at the National Institutes of Health. Only 4.4% of the 2006 National Institutes of Health budget will be devoted to the National Institute of Child Health and Human Development (NICHD). We are also in single digits regarding the pay line at NICHD, which was at the 20th percentile in 2003, then at the 14th percentile in 2005, and it is currently reported to be approximately at the 7th percentile. This scarcity of resources is certainly one of the primary challenges we face in pediatric research today.

What about global visibility? Well, Antarctica certainly has an image problem. When deciding at which pole he should set up shop, Santa chose the North Pole and not the South. The only marathon run under arctic conditions also chose the North Pole. Antarctica doesn't even have its own unique name. Antarctica is the "opposite of Arctic." At least pediatrics has name recognition. In Antarctica the numbers of

inhabitants are so few that it doesn't even make the map of the world's population distribution. At its peak in the summer there are only slightly over 4000 inhabitants on Antarctica, and the population certainly thins out when winter hits. On the global map of physician-scientists, the population of pediatric investigators is also relatively small in number. For example, in the American Society of Clinical Investigation's roster of 2800 members, there are only 234 from pediatrics. This signifies that there are either relatively few of us, that our voice is relatively inaudible for one reason or another, or both.

What about sense of direction? In Antarctica, even with blinding white terrain to the north, east, south, and west, there are occasions when the weather and the choices of direction are clear. However, at other times storms come up and it is easy to get lost. Similarly, in our research the potential directions to take are often multiple but at least readily apparent to us, yet at other times the scientific choices are instead absolutely perplexing. When the weather is clear, Antarctica is one of the few places on earth where actual mirages occur because the air is sufficiently pure to allow there to be 0% humidity. Similarly, in our research what we perceive to be truths often are later proven to be incorrect, so in all cases confirmatory strategies and frequent reassessments are mandatory.

Next let's consider the status of the stakeholders and the guiding principals for life on Antarctica and life in pediatric research. The 42 signee nations of the Antarctica Treaty at their first meeting in 1959 recognized that no individual nation can claim exclusive ownership of any portion of Antarctica, and they set forth three major guiding principals. They were that all acts on Antarctica are to be peaceful in purpose, that there is absolute freedom of scientific investigation, and that free exchange of information and personnel is mandatory. Similarly, no one can claim ownership of pediatric research, and freedom of investigation, cooperation, information, and personnel exchange guide our research activities.

Although the terrain is rough and the resources are scarce, although the global visibility is modest and the sense of direction is at times perplexing, the concept of universal ownership and the priority placed on intellectual freedom are shared reasons why the continent of Antarctica and the field of pediatric research warrant great respect and long-term preservation. The preservation of Antarctica is absolutely vital from an environmental standpoint. Even the conservative scientists who aren't panicking about global warming inform us that if the ice of Antarctica were to melt, it would raise sea level by

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200 m, which is enough to wipe out all coastal areas in the rest of the world. Likewise, any loss of current forward momentum in pediatric research would be tragic and far-reaching, going well beyond the adverse direct impact that would occur on the well-being of infants and children. Now more than ever it is apparent that both the genetic and the environmental factors which govern physiology and pathophysiology over the course of a lifetime have their greatest influence during fetal and early postnatal development, thereby programming the future quality of health of the individual. To give but one example, it is now estimated that the prevalence of childhood obesity is as high as 30%. If pediatricians are not provided with the tools to understand and reverse this frightening problem, the current generation of children will be the first in two centuries to have a shorter life expectancy than their parents. The tidal wave induced by continued insufficient support of pediatric research would simply be devastating.

Now recognizing that preservation is absolutely vital and that one of the major current challenges is the scarcity of resources, whose example should we follow if we are to have a positive impact? Be it related to Antarctica or pediatric research, certainly it should not be that of mere visitors, who may loudly claim importance as explorers or pioneers but then quickly leave without making a long-lasting contribution. That was the case for Ernest Shackleton, who was a famous Antarctic explorer in the early 1900s. Before his most well-known expedition to Antarctica aboard the ship *Endurance*, the “Want Ad” he placed in the London newspaper supposedly read, “Men wanted for hazardous journey. Small wages, bitter cold, long months of complete darkness, constant danger, safe return doubtful. Honor and recognition in case of success.” Does this sound like a fellowship director on truth serum? Reportedly Shackleton was a little too eager and uninformed about his planned route. Along with a crew of 27, Shackleton steered his ship directly into an ice pack where it was ultimately crushed, and it took the party 20 months and many near-death experiences before they escaped the continent. Talk about planning ahead for an experiment!

So the strategies taken by visitors simply are not helpful. Instead, we should pay close attention to the adaptations made by indisputably successful long-term inhabitants. On Antarctica this is the emperor penguin, made famous by the recent film “The March of the Penguins” (Fig. 1A). The emperor penguin is optimally prepared for the conditions he or she will face in the environment. The emperor penguin has 70 feathers per square inch, thick layers of down and blubber for insulation, a large amount of body oil to keep dry, and countershading such that they are lighter in color on the belly and darker in color on the back to provide camouflage when in the water. These attributes are pragmatic and not at all flamboyant, allowing the emperor penguin to be the only year-round inhabitant of the Antarctic ice. In contrast, just think how long a proud peacock would last at -140°F ! The pediatric physician-scientist-to-be should prepare for the upcoming environment and emulate the penguin, and not the peacock.

However, the long-term success of the emperor penguin does not lie in its individual armor against the cold and severe weather. Instead, it lies in the clarity of priorities of the group.

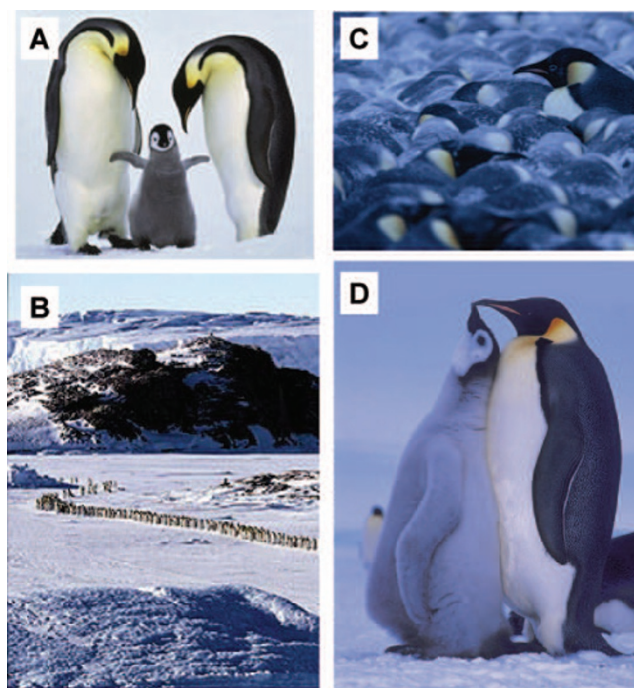


Figure 1. (A) Emperor penguin chick and its parents. (B) March of emperor penguins to breeding site. (C) Emperor penguins in a huddle (“turtle”) during a snowstorm. (D) Emperor penguin and its thriving chick. Photo credits: A, D: emperor-penguin.com; B, C: Jérôme Maison. © 2005 Bonne Pioche Productions/Alliance De Production Cinématographique.

These include an annual winter journey to the nesting site in which all members participate, displaying uniformity of purpose. In contrast to virtually every other bird on the planet that nests in the spring, the emperor penguin purposefully breeds during the harshest season so 5 months later when the chicks are ready to be independent, the conditions are far more favorable. The journey to the nesting site entails a 70–150 mile march (Fig. 1B), which, considering the length of stride of the penguin, is equivalent to 350–750 miles for humans.

Once at the nesting site, the male and female have shared equal responsibilities. One can’t help but immediately think of the clinical and research mentors during fellowship training, who should be equally empowered and equally responsible for a successful training experience. For the adult penguins the duties are divided, and both care for the egg and the chick. The male incubates the egg on top of his feet in a structure known as a brood pouch for 72 d, while the female returns to the sea for food. For the sake of the future of the group, sacrifice by the adults is a given. While spending the winter at the nesting ground, for the sake of the young, the male does not eat for 4 months and loses over 50% of his bodyweight. He feeds the chick “milk” produced by a gland in the esophagus.

This period of starvation of the adult male, which is unequalled on the planet, is only possible because when the adults are in the ocean they have unparalleled skill procuring food. They swim incredibly fast, reaching speeds up to 60 km/h. The male is capable of diving deep, up to $\frac{1}{2}$ km, and remaining in the deep for as long as 15 min in search of food. Great hunger is likely to be a helpful motivator. In similar fashion, we in pediatric research cannot thrive if our only

strategy is to adapt to merely survive the inevitable periods of resource limitation. We must also have great skill procuring resources, doing so by being unabashed in our efforts to promote our endeavor, by diving into uncharted areas to obtain resources, and by using our hunger as a powerful tool.

During mid-winter when the temperature plummets to its lowest level and storms are prevalent, the nesting penguins survive in groups known as turtles (Fig. 1C). The turtles prevent heat loss and can be as dense as 10 penguins/M². The adults take turns standing at the periphery, and are cautious in their movements. Panic movements while in the turtles can lead to the loss of hundreds of eggs because an egg out in the midwinter Antarctic air will freeze in 2 min. Likewise, when conditions are challenging for us in pediatric research, our best strategy is to recognize the strengths of interaction with our peers, to take turns weathering the storms that we face, and to most importantly avoid panic at the risk of losing the most vulnerable amongst us, which are those who will be the guardians of our field in the future.

Some may wonder why face the storm, why be foolhardy enough to “stay on the ice”, if you will, year-round. Well, we do so because we know that spring always comes, and the young who have been nurtured through the harsh times can then have the opportunity to suddenly realize that it is safe to venture out, that there is absolutely no feeling like spreading your experimental wings, that it is invigorating to join one’s colleagues, and that with perseverance and support and nurturing, they will have their day in the sun. The multiple research honors that we awarded to students and trainees and young investigators during the SPR Presidential Plenary Session today are firm evidence of the success that comes from perseverance and nurturing, and we should be energized by witnessing them.

Spring is also a delightful time for the mature of the species. It is a time when there is freedom to fly, which in research terms means a time when one can test that new provocative concept, the idea that may blow open an entirely new area of investigation. It is also a time when long-term, high-impact contributions can be recognized, as has occurred during the SPR Presidential Plenary Session with the E. Mead Johnson Award presentations. Spring is also when satisfaction is felt because the nurturing has been successful, allowing the young chick to thrive to become as tall as mom or dad so that it is very much time to part company (Fig. 1D). The conditions are now optimal. The ocean is not 70 to 150 miles away, but just hundreds of yards away, and the chicks are ready to be on their own.

Survival through the dark, incredibly cold winter to spring-time is impossible for the penguin that stands alone. Similarly, the lone individual engaged in pediatric research will not fare well, and both are in peril if they do not recognize that there is true strength in numbers. In pediatric research, this recognition by the individual, be they a trainee or a PI, is the first key to success during challenging times. Interactions with others in science, either near or far, within pediatrics or well beyond it, that ensure that one’s research activities entail only state-of-the-art concepts and scientific strategies are simply vital. Another key to success during challenging times is that our home institutions must rediscover certain aspects of the

concept of strength in numbers. Now more than ever, programmatic approaches that transcend classical boundaries of subspecialties or departments should be prioritized and supported. In addition, effective engagement in multicenter research networks or colloquiums pursuing hypothesis-driven investigation should be valued and encouraged by our institutions. As importantly, organizations such as the Society for Pediatric Research must foster the benefits that come with strength in numbers.

I am delighted to report that the SPR is doing exactly that with two new initiatives. The first is the Society for Pediatric Research Research Conference, or SPRRC. This was first proposed by Dr. Lisa Guay-Woodford during her SPR presidency in 2004–2005. SPRRC is a small, theme-based, biannual research conference focusing on new scientific advances. The SPRRC is designed to foster investigative interactions and the development of research networks, to encourage interdisciplinary exchange, to facilitate the development of focus groups that transcend institutional or geographic boundaries, and to expose young investigators and trainees to top-tier scientists active in pediatric research. The procedure to initiate the first SPRRC began with the solicitation of proposals. Fourteen proposals were received, and the SPRRC review committee consisting of SPR members from various disciplines chose the most worthy proposal. The 2007 SPRRC is entitled “Early Nutrition, Interactions with the Gastrointestinal Microenvironment and the Innate and Adaptive Immune Systems: Mechanisms of Effects on Subsequent Health.” The organizers are Drs. Joseph Neu, W. Allen Walker, Bill Hay, and Patti Thureen. The 2007 SPRRC will take place October 17–19, 2007, in The Woodlands, Texas.

The second initiative is to compile an electronic database known as DOOR (Database Optimizing Outreach in Research). This is a joint venture between the SPR and the APS. SPR and APS members will designate the areas of their research interest and expertise in an easy format in the DOOR which will be available on the SPR and APS website. Once compiled, any SPR or APS member can enter the DOOR and perform a search to obtain the names of colleagues with specific research interest or expertise, their email address, their laboratory or clinical research program web page, and their publications and grants *via* Pubmed and the National Institutes of Health CRISP database. Both the access to the DOOR and the interactions which can ensue through it can occur 24 h a day, 7 d a week, and 365 d a year. With the DOOR, colleagues within the SPR gain instant access to you and your research program, new research networks can be developed, and it will be possible to collaborate with fellow researchers around the world and establish new interest groups. The interactive features of the DOOR are being finalized, and we are excited to anticipate its rollout in the near future.

So, what is the cold, hard truth about pediatric research? Well, the truth is that like Antarctica, pediatric research is incredibly unique, and it is vital. Like Antarctica, one of the major challenges to pediatric research is currently a scarcity of resources. If we learn from the clever, properly-prioritized adaptive behaviors of the emperor penguin, we can weather

the storm of current resource limitations by recognizing the strength in our numbers. Through our efforts, the sun will always shine on pediatric research. In Antarctica during the coldest season, during the total darkness of the peak of winter, the refraction of light on the lower layers of the atmosphere makes it possible to see the sun even when it is below the horizon. Likewise, there are truly never dark times for pediatric research, only times such as the present day that challenge us to remember that the sun is always there, and to recognize the strength that we gain in our numbers.

In closing, I would like to recognize those who have provided me with sunlight during my career to-date in pediatrics. Dr. Reggie Tsang introduced me to biomedical research during residency, Dr. Bill Oh cultivated that interest during my fellowship, and Drs. Joe Warshaw and Charles Rosenfeld

allowed me to be a student during my early years on the faculty at the University of Texas Southwestern Medical Center. Dr. Chuck Ginsburg saw the value of perpetual student status, and most recently I am thankful that Dr. George Lister has encouraged me to think programmatically and develop a new research division. During my tenure as SPR President, the sunlight has been provided by the multiple talented individuals in the Central Office led by Ms. Debbie Anagnostelis and Ms. Kathy Cannon, and by my fellow SPR Council Members, in particular our Secretary-Treasurer Dr. Mark Schleiss. The broadest rays of sunlight come from my wife and my best friend Mary, whom I can never thank enough for her love and encouragement, and from our two chicks, Brian and Katherine.

Thank you all so much.