

# Genetic predisposition to breath-hold diving induced Pulmonary Edema

Hold your breath: DAN Europe received a prestigious recognition for their work in the field of apnea diving, thanks to valid findings in the correlated genetic research. Now you can breathe again: DAN Europe's work in this field will continue to go deeper!

One of the problems faced by many apnea divers (around 26%) is the development of pulmonary edemas caused from practicing their favorite activity. The topic is becoming more and more present in social media and chat rooms among underwater fishermen. Even Mr. Danilo Cialoni, Coordinator of DAN Europe Foundation's department of Research Techniques Development and also a passionate apnea diver and instructor, suffered from it, as he described in a text box in the latest book by Umberto Pellizzari ("Specific Training for Apnea. Deep Apnea, Static and Dynamic," Addictions-Magenes Editoriale, 2014): "As I continued to improve my apnea performance, I started noticing the presence of some blood in my saliva at the end of each training session. The phenomenon grew continuously more noticeable and more bothersome; no one could give me any trusted information, and the data available to the scientific community was almost nonexistent. One day, the problem was much more evident and traumatic... The training session was over but I had to return to the bottom, at 36 meters, to free the anchor of the accompanying boat. In the end, I managed to do it, but I immediately realized that something bad had happened to me. During surfacing the strange feeling worsened. At the surface it felt like there was no air in the atmosphere, and for each breath, oxygen was never enough. It was hard to overcome this shortness of breath, and it took me a while to breathe normally again. In the emergency room, less than an hour later, my coworkers at the hospital had me undergo a CAT scan, allowing them to see the condition of my lungs, which were full of blood, extravasated during my effort at the bottom and also due to equalizing during the descent. My case was so severe and rare that, instead of the usual recovery that takes a few hours, it took 3 days for my lungs to return to normal and over 3 months for total recovery."

## The Research

In the years following this incident, Mr. Cialoni passionately dedicated himself to understanding the real mechanism that provoked it, and thanks to numerous research collaborations with DAN Europe, other authorities, Universities and training organizations, he was able to carry out many tests on apnea divers. Now a clear picture began to take shape. Essentially, the pressure at depth causes the blood in the lungs to engorge, a phenomenon that is called blood-shift and is very similar to what happens during extreme exertion or high-altitude hypoxia. This phenomenon is well known and studied in other fields. In test after test, research has shown that pulmonary edema in divers is linked to an increase in pulmonary pressure, and all measures that cause a rise in intrathoracic pressure, such as equalization, make the situation worse. Some subjects, who are predisposed, cannot withstand the rise in pressure quickly enough and they develop a pulmonary edema, which is "non-cardiogenic" because it is not caused by heart disease.

Mr. Cialoni just had then to understand how to know whether a subject is predisposed or not. Understanding the phenomenon made it possible to discover that gradual adaptation and proper heating could drastically reduce the symptoms, just like it happens with acclimatization for mountaineers. These practices are good precautions for all apnea divers, but they need to become the rule for those who are prone to pulmonary edema.

At this point, the innovative idea was to break down the wall: rather than devote time to a research on

phenotypes (the observable characteristics of an organism), better to directly analyze the “software” that controls the human body: genomes. This resulted in a research project conducted in collaboration with Prof. Alessandro Marroni and Mr. Max Pieri of DAN Europe Research, Prof. Nicola Sponsiello and Mr. Vittorio Lucchini.

The scope of this study was to identify the polymorphisms that indicate a higher risk factor in those who have them. The investigated polymorphisms were those associated with the production of enzymes that regulate pressure in blood vessels. Subjects who have the “good” variant of these genes are able to better sustain the increase in lung pressure caused by blood-shift, and they have a lower risk of pulmonary edemas.

The study focused particularly on two variants of the gene for the Endothelial Nitric Oxide Synthase enzyme (eNOS): The G894T, which assists in the regulation of vasodilation, blood flow and blood pressure, and the T786C, associated with pathogenesis of heart disease. Variants of the converting enzyme *angiotensin* (ACE) were also studied. All three investigations showed a significant rise in the risk of developing a pulmonary edema, as explained in the publication, “Genetic predisposition to breath-hold diving induced Pulmonary Edema: Up-Date,” written by the same researchers, of which Mr. Cialoni is lead author.

These studies and their subsequent publication were greatly recognized during the annual EUBS (European Underwater and Baromedical Society) meeting in Wiesbaden, where the authors were awarded the acclaimed “Patrick Musimu Award 2014.”

### **What will change for apnea divers?**

The outcomes of this study in the apnea diving world are revolutionary. It is now enough to take a genetic test to know one’s predisposition to pulmonary edemas. DAN Europe has already made available a quick and simple method for taking the test: the apnea diver is provided with a tube with a closed cap and a cotton swab inside. The diver just needs to open the tube, swab his/her inner cheek, and close the tube... just like you see on TV crime series. This is to gather some cells on the inner wall of the cheek; cells which will be tested by a genetic testing agency in order to analyze DNA to obtain a genotype. The report will let the apnea diver know if he/she is at risk of developing a pulmonary edema. Having investigated three different polymorphisms, of course there will be some unlucky subjects who possess all “bad” versions of the genes, and lucky ones who have “good” versions of all three, but most of the apnea divers’ results will be mixed.

This does not mean that those who are less at risk should not take any precaution. The real goal is to inform those who are more prone to pulmonary edemas that they need to focus more on reducing external risk factors; proper heating can make up for the diver’s less-than-optimal genotype.

Another step forward may come from a new study that DAN Europe has started, which means to make up for the lower production of nitric oxide in people with a non-optimal genotype through specific and personalized nutrition plans. The study looks at how diet can lower the risk of developing a pulmonary edema for those who are prone to it, and possibly put them at the same level as those “lucky” divers who are not predisposed. A new branch of science is born at DAN Europe, that of “nutrigenetics,” and it will fully become a part of the diving world!

### **DAN Europe and Apnea Diving**

In addition to scientific research, DAN Europe takes care of divers in terms of emergency management, by

setting up low-cost and simple insurance policies for apnea courses and training, in addition to those already provided for sports divers. The policies cover all activities of apnea diving: general apnea diving, underwater fishing, and static and dynamic apnea diving competitions. There are three levels of courses: Apnea Entry (beginner-level courses up to 30 meters deep), Apnea Advanced (second-level courses up to 30 meters deep) and Apnea Specialty (specialization courses up to 40 meters deep). There is also an Apnea Training week-long insurance policy, which also covers the use of the sled, and applies to depths of up to 100 meters for variable weight apnea and 70 meters for constant weight apnea.

DAN Europe and apnea divers continue “arm in arm” on the path to make diving into an activity that is always more enjoyable, safer and more... breathtaking!