Executive summary of a research project

Widespread episodic thiamine deficiency in Northern Hemisphere wildlife

Thiamine (vitamin B_1) deficiency is a far more widespread problem than previously realized. This is shown in a new extensive scientific work by researchers from 5 countries and 13 universities and other research institutions in Europe and North America, coordinated by Professor Lennart Balk at Stockholm University. By conducting chemical and biochemical analyses of thousands of mussels, birds, and fishes in 45 areas in the Northern Hemisphere, the researchers now conclude that thiamine deficiency seriously affects these groups of animals across a huge geographic area. Because the investigation has been conducted for several years it has also been concluded that the thiamine deficiency occurs episodically, i.e. that it may appear for one or more years in an area, after which it can disappear for some time and then return.

It is well known that thiamine deficiency causes mortality in animals. Now, however, special attention needs to be paid also to the high prevalence of other effects of thiamine deficiency, including impaired health and reproduction, which are not directly fatal. In the long run, also these 'sublethal' effects can cause populations to decline and disappear. Examples of sublethal effects related to thiamine deficiency include reduced growth, altered organ sizes, generally impaired nutritional status, impaired blood chemistry, increased infections, altered behaviour, impaired swimming endurance, and substantial negative effects on reproduction. The link between such effects and thiamine deficiency has previously been demonstrated in laboratory experiments with several animal species, but now also in wildlife in the field.

The species in the Northern Hemisphere investigated here, and in which thiamine deficiency has been demonstrated, are blue mussel, common eider, American and European eel, Atlantic salmon, and sea trout. Moreover, data in the existing literature have been revisited and, in the light of the new results, contributed to a more precise view of the occurrence of lethal and sublethal thiamine deficiency across the Pacific Ocean, North America, the Atlantic Ocean, and northern Europe.

A male common eider brakes in order to land on the water. Photo: Lennart Balk

All thiamine in the food web is produced by the green plants and by certain fungi and bacteria, whereas all animals must obtain thiamine via their food. In the living cell, thiamine diphosphate acts as a cofactor for at least five thiamine-dependent enzymes, of which transketolase and α-ketoglutarate dehydrogenase have been analysed here. These life-sustaining enzymes, which are active in the basic cellular metabolism, are non-functional if the cofactor is missing. Just as other biomolecules, thiamine is a possible target for noxious influence by environmental disturbances.

Thiamine deficiency was demonstrated in the investigated animals as reduced thiamine concentrations (chemical analysis), reduced activities of the thiamine-dependent enzymes (biochemical analysis), and increased proportions of these enzymes lacking the cofactor thiamine diphosphate (biochemical analysis). Thiamine deficiency was also demonstrated by the fact that thiamine treatment improved the thiamine status of individuals. This is because thiamine treatment should have no effect at all on non-thiamine-deficient animals, where any excess thiamine is just excreted.

Dead blue mussels washed up on the shore. Photo: Le Carlsson

This is the first time that thiamine deficiency is demonstrated in blue mussels with both chemical and biochemical analyses. At times, there was also a strong relationship between the thiamine status of blue mussels and their condition. When the thiamine content in blue mussels from the Baltic Sea was compared with various doses of thiamine in the food of birds in a controlled laboratory experiment, it was found that the thiamine dose that would be obtained by eating blue mussels from the Baltic Sea would result in severe thiamine deficiency. Hence, it is highly likely that the thiamine deficiency observed in wild common eiders is caused by thiamine deficiency in its main prey (blue mussels). It is, in other words, alarming that the thiamine concentrations in the blue mussels in the Baltic Sea and certain areas in Iceland today are so low that mussel feeding fish and birds – not only common eiders – are at risk of being injured by insufficient thiamine content of the blue mussels. An important

observation is also that the blue mussels in the Baltic Sea today do not have a generally lower flesh content compared to that observed in investigations performed 40 years ago. Hence, it is unlikely that the recent population declines of many mussel-feeding species would be caused by lower flesh content in the blue mussels, whereas many observations indicate a risk to suffer from specific deficiency of thiamine.

Analyses of both American and European eel showed that the thiamine concentrations in organs and tissues are much too low, maybe just one fifth of what is needed to support both migration to their spawning areas in the Sargasso Sea and successful reproduction with healthy offspring. This thiamine deficiency may, by itself, explain the dramatic declines of eel populations in the Northern Hemisphere during the last few decades. It is also probable that other effects of thiamine deficiency now observed in the eels – e.g. reduced growth, low condition, and impaired immune defence – occur analogously in other species of fish and birds in the affected regions.

Investigations performed from the mid-1990s and onwards have repeatedly demonstrated severe thiamine deficiency in salmonines in North America and northern Europe. These investigations have predominantly focused on direct mortality in the offspring, i.e. embryo mortality in the eggs and larval mortality during the stage of yolk sac consumption. In the present investigation, special attention is paid to sublethal effects in both parents and offspring. It is concluded that the effects of thiamine deficiency are severely underestimated when the focus is limited to direct mortality. In previous investigations of salmonines, it has often been found that the limit for direct mortality in the offspring is at a thiamine concentration in the eggs of ca 4 nanomol thiamine per gram egg. In the present investigation, it is shown that the limit for sublethal thiamine deficiency probably is at ca 18 nanomol thiamine per gram egg, i.e. much higher than the limit for direct mortality. In summary, this means that a much larger proportion of the populations of various salmonines suffer from detrimental thiamine deficiency than previously realized.

In the present investigation, it is concluded that the thiamine deficiency occurs with variable intensity in time and space. For example, the Swedish Baltic Sea coast (Baltic Proper) seems to be much more affected compared with several areas in Iceland. The gravity of the current situation is also heightened by the finding that many investigated individuals apparently had a thiamine status that was on the margin for their survival.

The overall goal of the research is to find the underlying cause(s) for the thiamine deficiency, i.e. how it has arisen in the ecosystems. The current results provide knowledge to support the further investigation of possible biochemical mechanisms. This basic knowledge includes the distribution of the thiamine deficiency in time and space, as well as among various species. Such information will lead to an integrated picture of causal relations and facilitate the prioritization of candidate mechanisms for more detailed evaluations of causality.

Currently, it cannot be excluded that the observed thiamine deficiency is substantial enough that it is significantly contributing to the ongoing worldwide extinction of many animal species. Other researchers have pinpointed this loss of biological diversity as the most serious of all threats to life on earth today.

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More information

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Ett drygt dussin nyckelreferenser för tiamin och tiaminbrist I vårt ekosystem. Listan är inte 100%-ig beskrivande men utgör en bra start för kunskapsläget.

Upptäckten av att laxfiskar saknar tiamin för dess överlevnad och reproduktion, samt att det just är tiamin specifikt som saknas;

Fitzsimons, J. D. The effect of B-vitamins on a swim-up syndrome in Lake Ontario Lake trout. Suppl. J. Great Lakes Res. 21, 286–289 (1995).
Åkerman, G. & Balk, L. Descriptive studies of mortality and morphological disorders in early life stages of cod and salmon originating from the Baltic Sea. *Am. Fish. Soc. Symp.* 21, 41–61 (1998).

Påvisad tiaminbrist i tre ytterligare klasser av djur, nämligen reptiler, musslor och fåglar, samt även i icke laxfiskar;

Sepúlveda, M. S. *et al*. Organochlorine pesticides and thiamine in eggs of largemouth bass and American alligators and their relationship with early life-stage mortality. J. Wildlife Dis. 40, 782–786 (2004).
Balk, L. *et al*. Wild birds of declining European species are dying from a thiamine deficiency syndrome. Proc. Natl. Acad. Sci. USA 106, 12001–12006 (2009).
Balk, L. *et al*. Widespread episodic thiamine deficiency in Northern Hemisphere wildlife. *Sci. Rep.* **6**, 38821; doi: 10.1038/srep38821 (2016). (www.nature.com/articles/srep38821)
Mörner, T. *et al*. Thiamine deficiency impairs common eider (Somateria mollissima) reproduction in the field. Sci. Rep. 7, 14451; doi: 10.1038/s41598-017-13884-1 (2017).

Internationella forskar-symposier, sammanfattande volymer, som visar på olika aspekter av laxfiskars pågående tiaminbrist (exempelvis immunsystem påverkan) i Östersjön och i Nordamerika;

McDonald, G., Fitzsimons, J. D. & Honeyfield, D. C. (eds.). Early life stage mortality syndrome in fishes of the Great Lakes and Baltic Sea, American Fisheries Society, Symposium 21 (1998).
Bengtsson, B.-E., Hill, C., Nellbring, S. & Kessler, E. (eds.). Reproductive disturbances in Baltic Sea fish: An international perspective, Ambio 28(1) (1999).
Blazer, V. S. & Brown, L. L. (eds.). Early mortality syndrome in Great Lakes salmonines, Journal of Aquatic Animal Health 17(1) (2005).

Påvisad tiaminbrist i havet;

Sañudo-Wilhelmy, S. A. et al. Multiple B-vitamin depletion in large areas of the coastal ocean. Proc. Natl. Acad. Sci. USA 109, 14041–14045 (2012).

Review artikel om tiaminets betydelse och effekter vid brist;

Manzetti, S., Zhang, J. & van der Spoel, D. Thiamin function, metabolism, uptake, and transport. *Biochemistry* 53, 821−835 (2014).

Effekter på en laxgrupp under vandringen i älven när de har tiaminbrist;

Fitzsimons, J. D. *et al*. The effect of thiamine injection on upstream migration, survival, and thiamine status of putative thiamine-deficient coho salmon. *J. Aquat. Anim. Health* 17, 48–58 (2005).

Human tiaminbrist, långsiktiga skador på viktiga funktioner i hjärnan;

Fattal-Valevski, A. et al. Outbreak of life-threatening thiamine deficiency in infants in Israel caused by a defective soy-based formula. Pediatrics 115, e233–e238; 10.1542/peds.2004-1255 (2005).
Mimouni-Bloch, A. *et al*. Thiamine deficiency in infancy: Long-term follow-up. *Pediatr. Neurol.* 51, 311–316 (2014).

Ytterligare information

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