

Histamine Intolerance

Histamine and
Seasickness

Reinhart Jarisch
Editor

 Springer

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Translation from the German language edition: Histaminintoleranz by Reinhart Jarisch Copyright
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Illustrations: Hippmann GbR, Schwarzenbruck

ISBN 978-3-642-55446-9 ISBN 978-3-642-55447-6 (eBook)
DOI 10.1007/978-3-642-55447-6
Springer Heidelberg New York Dordrecht London

Library of Congress Control Number: 2014947231

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Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

Preface 1

An incredible fact: 12 years have elapsed since the first German edition. The second edition had to be reprinted eight times.

It is an opportune moment to present the third edition with the most recent results of our research.

The investigation of seasickness in the German navy has been concluded, and has confirmed the efficacy of vitamin C chewable tablets.

A study concerning the significant condition of the irritable bowel has been completed.

Wine enthusiasts will be glad to read about the most recent results of our investigations in regard of red wine, sparkling wine and champagne. Particularly our analyses on red wine in respect of other biogenic amines have yielded exciting data. Some wines are marked by a typical distribution pattern, similar to the fingerprint in the study of crime. Some biogenic amines are responsible for the poor quality of wine, which makes it possible to identify certain poor-quality wines in the laboratory.

Wasp venom allergy is gaining increasing importance in recent times, especially because of rising death rates in recent years. These deaths are caused by anaphylactic shock.

Death rates are even higher among drug addicts, and probably also caused by anaphylaxis. In Austria alone, more than 200 persons died last year of drug abuse. The major significance of histamine research is illustrated by the fact that opiates like heroin release histamine.

By performing investigations in drug addicts we showed that the risk of anaphylaxis can be determined in advance. Thus, these investigations benefit other persons as well.

Last but not least, studies in patients who received specific allergy vaccination have proven the value of antihistamine premedication, which we have been using for several years now. It enhances the safety of treatment.

Antihistamine premedication was specifically included in the list of measures to prevent anaphylactic shock at the 2012 annual meeting of the American Academy of Allergy Asthma and Immunology (AAAAI) in Orlando.

The contents of the individual chapters have been updated and significant new results of research have been incorporated in this edition.

We have come another step closer to the aim of good health by expanding our knowledge and improving therapies.

Vienna, Austria
February 2014

Reinhart Jarisch, MD

Preface 2

... on Chapter 10 *by Wolfgang Hausner*

Sometime in the distant past, Man first ventured upon the sea and started to sail. When this occurred is rather uncertain, but we may assume with certainty that seasickness became apparent at this point in time.

Not all persons are affected by seasickness. In fact, the term itself is flexible. It is not as clearly defined as pregnancy, for instance. One is either pregnant or one is not.

Thus, two persons may assert, with good reason, that they are seasick: one experiences nausea for a short period of time, vomits a little, and feels much better afterwards, whereas the other vomits the living daylight out of his body and the stomach feels like an open wound tortured by regular and painful seizures. The person's regurgitations consist largely of gastric acid, the throat feels burned, and tears well up in the eyes.

A proverb sums up this pathetic condition quite aptly: One first fears one will die, and then fears one will not.

Over the years, several substances to counteract this condition have been tested and introduced in the market. Some alleviate the condition and are frequently associated with side effects, but a universal remedy does not exist.

Prof. Dr. Reinhart Jarisch has achieved a genuine breakthrough in this field. He has shown that the primary cause of seasickness is histamine – a fact that was not recognized until now. This information alone will not make a seasick person healthy, but Dr. Jarisch does not merely tell us why we become seasick. He also has a formula at hand which is simply astounding. I hope it will be utilized by as many persons as possible.

Austrian World Circum Navigator

Wolfgang Hausner

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Reinhart Jarisch

Headache is usually assigned to the cervical spine or the weather. Laborious investigations such as X-rays of the cervical spine, computed tomography, or magnetic resonance tomography are used to determine the cause of the condition. In other words, we still live in a static rather than a dynamic age: pathophysiological changes are simply ignored. Consequently, patients are issued a normal report although they are ill and in turmoil.

A blocked nose is believed to be related to a deformation of the nasal septum, although 40 % of the population have this anatomical variant and many of them have no symptoms. A running nose is assigned to allergy even when allergy tests are negative. This occurs although we are well aware of the fact that some persons experience a “blocked nose” when they consume wine.

Bronchial asthma may be caused by so-called exogenous factors. In other words, it may be caused by environmental factors such as the house dust mite, pollen, epithelial tissues of animals, and mildew. It may also be caused by endogenous factors (arising from within) – also known as intrinsic factors – of unknown origin. Many patients have been long aware of the fact that red wine and even Emmental cheese or pizza with tuna fish may cause shortness of breath.

Furthermore, some drugs are inhibitors of diamine oxidase, which is the enzyme that degrades histamine and is specifically used for the treatment of asthma. This approach is used although we are well aware of the fact that histamine provocation is employed to obtain evidence of bronchial asthma and a positive test result helps to diagnose bronchial asthma.

When faced with gastric symptoms, the clinician performs gastroscopy in order to demonstrate the *Helicobacter pylori* bacterium, although a histamine-free diet would clarify the situation much more rapidly and economically.

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Cardiac arrhythmia in young adults gives rise to extensive cardiological investigations, usually with a negative outcome, followed by a statement to the effect that the patient is fine. However, the patient knows this is not the case.

Diarrhea and soft stools are a reason to perform an X-ray investigation of the bowel and laborious examinations of the bowel, many of which can be quite embarrassing and usually yield a negative result. One does not consider the fact that food intolerance might be a part of the problem. Even patients with Crohn's disease are simply given drugs, without taking the option of a histamine-free diet into account.

Low blood pressure is a typical symptom of histamine intolerance but is still accepted as "the will of God" in most cases. Besides, some drug allergies are actually an expression of histamine intolerance. Even patients with neurodermitis may suffer from it and may benefit from a histamine-free diet.

This book does not intend to invent a new type of medicine. Rather, it intends to fill a gap in medicine which has been pervaded by alternative medicine. The latter has been a clinical failure but a financial success in this sector. This book will help to explain medical processes in the style of Hugo Portisch (a very successful Austrian journalist who is able to explain complex matters of foreign policy in a way that any person would understand them) and to demonstrate a simple way of implementing those facts which patients are frequently aware of unconsciously.

Reinhart Jarisch, Felix Wantke, Martin Raithel,
and Wolfgang Hemmer

2.1 Histamine

Reinhart Jarisch

Histamine is a simple chemical substance with a molecular weight of 111 Da. It was discovered in the ergot in 1911. Many great discoveries in medicine are based on coincidences, errors, or sheer carelessness. This is true of histamine as well. Several years later it was discovered that the ergot investigated at the time was contaminated with histamine-producing bacteria and the ergot itself does not contain histamine.

This discovery is important in that it can be immediately extrapolated to food-stuffs. In other words, those types of food that undergo a process of maturation involving bacteria naturally contain high levels of histamine. In order to minimize the production of histamine in red wine while it is undergoing fermentation, one has now started to use cooled vats because bacteria grow faster at high temperatures and more slowly at low temperatures.

Histamine is the principal mediator (inflammatory substance) in allergic diseases such as allergic rhinitis (hay fever) or bronchial asthma. Besides, histamine is the classic triggering substance for urticaria (hives) and plays an important role in drug allergy and drug intolerance.

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2.1.1 Physiological (Natural) Effects

The human body produces histamine, which stimulates the secretion of gastric juices. Histamine has a vasodilating and therefore antihypertensive effect and acts as a neurotransmitter in the circadian rhythm and in controlling appetite, learning abilities, memory, emotions, neuroendocrine regulation, and immunomodulation.

Undesirable effects include headache, a blocked or runny nose, respiratory obstruction leading to bronchial asthma, tachycardia (rapid pulse), extrasystole (additional heart beats), even massive cardiac problems, gastrointestinal symptoms that may lead to soft stools or diarrhea, and low blood pressure (hypotension). Swelling below the eyelids is quite common. Urticarial exanthema (nettle rash) may occur occasionally. Histamine is produced by the human organism, is deposited in blood and tissue cells (basophilic granulocytes and mast cells), and is always available for immediate release. Besides, histamine may also enter the body from the outside. This occurs on the one hand through inhalation, such as during histamine provocation for the investigation of bronchial asthma, or orally by the ingestion of food or beverages containing histamine. After intestinal absorption, histamine reaches the bloodstream.

Histamine may also be injected into the skin during a so-called prick or intradermal test. It is known to cause wheals or erythema (reddening of the skin), similar to a mosquito bite.

Intravenous administration of histamine may trigger any of the above-mentioned symptoms. The most dreaded of these are splitting headaches, perceived by patients as a tearing sensation in the head.

While the reactions of histamine on the skin are rather harmless, such as itching or wheals, the entry of histamine into the bloodstream may have fatal effects.

A scientific investigation performed by Sattler and Lorenz (1990) elucidates this phenomenon. The authors investigated two groups of 15 pigs each, who were given a small quantity of alcohol and Emmental cheese through a gastric tube. One group of pigs was given an inhibitor of diamine oxide (a histamine-degrading enzyme, abbreviated to DAO) prior to this step. The group of pigs that received no previous treatment tolerated alcohol and cheese without difficulties. All pigs in whom the histamine-degrading enzyme had been blocked by medication experienced anaphylactic shock after the ingestion of alcohol and Emmental cheese; three pigs died. The experiment was then repeated. The pigs were again given an inhibitor of DAO, but additionally received an antidote in the form of drugs that could block the histamine receptor (H1 and H2 receptor blockers were administered). A small quantity of alcohol and Emmental cheese were then given, and the food containing histamine was tolerated without difficulty. Thus, it becomes obvious that histamine alone is not hazardous. Rather, it is the absence of appropriate degradation mechanisms that is responsible for the symptoms.

Stale meat contains large quantities of histamine. Very stale meat is known as carrion. It is tolerated without difficulties by animals like lions and even pigs. If humans were to eat such food, they would most certainly die. Lions tolerate such intake of histamine easily because their bodies have sufficient quantities of the histamine-degrading enzyme. The question that arises here is: Would it be possible

to increase the quantity of DAO in the human body and thus protect it specifically from allergic or allergy-like diseases?

There is a natural model for this phenomenon: pregnancy. During pregnancy a large quantity of DAO is produced in the placenta from the third month of gestation onward. The physiological purpose of this measure would be to protect the uterus (which is sensitive to histamine) from frequent exposure to histamine due to the ingestion of food. To ensure that the fetus is not passed out prematurely, the maternal body produces about 100–300 times more than the normal quantity of DAO. This protects the uterus from the effects of histamine and premature termination of pregnancy. It is also the reason why many allergic pregnant women report complete resolution of allergic diseases such as hay fever or asthma from the third month of pregnancy onward, which then return after delivery of the infant and expulsion of the afterbirth (also see chapter on Pregnancy and Allergy).

2.2 Diamine Oxidase

Felix Wantke

Almost every foodstuff contains histamine. The body has to protect itself effectively from histamine, which is a highly potent biological substance. Therefore, the first barrier to histamine exists in the intestine. The cells of the intestinal mucosa, known as enterocytes, produce and contain an enzyme which is able to degrade histamine (Baenzinger et al. 1994; Maslinski and Fogel 1991). The enzyme is known as diamine oxidase, has a molecular weight of 90,000 Dalton (Da), and contains copper. Diamine oxidase is mainly found in the small intestines, the liver, the kidneys, and white blood cells. In pregnant women, diamine oxidase is additionally formed in the placenta. Interestingly, pregnant women have about 100- to 300-fold higher diamine oxidase levels in the blood than nonpregnant women. Diamine oxidase is continuously produced and secreted into the intestinal lumen. Therefore, in a healthy person, histamine-rich food is largely eradicated of histamine in the intestine. The remaining quantity of histamine is degraded by diamine oxidase when it passes through the intestinal mucosa. Histamine is degraded into imidazole acetaldehyde and then into imidazole acetic acid. The cofactor of diamine oxidase is 2,4-trihydroxyphenylalanine quinone (McGrath et al. 2010).

Diamine oxidase is a sensitive enzyme. It can be inhibited by various substances, such as other amines, alcohol, its degradation product acetaldehyde, and various medications (Sattler et al. 1988, 1989). Several studies have shown that diamine oxidase is reduced in the presence of inflammatory bowel diseases. As mentioned earlier, diamine oxidase in the intestine is the first protective mechanism to shield the body from histamine in food. Diamine oxidase also protects the body from histamine formed physiologically by intestinal bacteria in the intestine (Sattler et al. 1988, 1989).

When histamine is absorbed despite these mechanisms, it is transported into the liver through the bloodstream. There, histamine is further degraded by N-methyltransferase, which is the second important histamine-degrading enzyme in the body. N-methyltransferase cleaves histamine into N-methylimidazole acetic