

Report of the Scientific Committee of the Spanish Agency for Food Safety and Nutrition (AESAN) on the risk of food poisoning due to the presence of biogenic amines in meals made from chicken meat consumed by children under 3 years of age

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Abstract

Biogenic amines are low molecular weight organic bases that come from the enzymatic decarboxylation of amino acids. They are present in many types of food, with the highest concentrations usually found in fish and their derived products, as well as in beverages and fermented foods of plant, meat and dairy origin. In general, the concentration of these amines increases as the hygienic quality decreases, so the presence and levels of biogenic amines provide indirect information on the degree of contamination and on food production, handling and storage practices.

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Meat and meat products are a group of foods that, due to their high protein content and the high probability of microbial contamination during slaughter and processing processes, favour the formation of biogenic amines that can appear in a wide range of concentrations. A high concentration of one or more biogenic amines suggests high microbial growth and, with it, poor food quality.

As a result of the appearance of a number of foodborne outbreaks in nursery schools in Spain, associated with the consumption of chicken meat with the presence of biogenic amines by children under 3 years of age, the Scientific Committee of the Spanish Agency for Food Safety and Nutrition (AESAN) has assessed the available information on the factors that can influence the appearance of this type of outbreaks; the acceptable levels of biogenic amines in chicken meat; those aspects related to the production of chicken meat that have an influence on the level of biogenic amines; the influence of the expiration time and storage temperature from the time of the slaughter of the chickens and the measures that can minimise the risk in the canteens that use this type of meat when the recipients are children under 3 years of age.

The Scientific Committee concludes that, due to its structure and protein composition, chicken meat is, after fish, the most susceptible to developing biogenic amines, with factors such as the use of a raw material of low hygienic quality and inadequate or very long transport and/or storage conditions having an influence on their appearance. There is no consensus on the levels of biogenic amines that could be used as a guide in foods. There are also a number of uncertainties regarding the toxicity of histamine and tyramine, such as the concurrence of both in the same food, or the potentiating effect that the presence of other biogenic amines may have. Therefore, it is difficult to establish safe maximum levels in this population group.

The primary production systems of chicken rearing do not seem to have a decisive influence on the levels of biogenic amines in meat. However, meat production and processing systems can have a great influence on the microbiological contamination of carcasses, which is a critical factor for the formation and accumulation of these amines in meat during its conservation and storage.

It would be advisable not to use chicken meat with a storage time of more than 5 days after slaughter of the birds in the diet of children under 3 years of age, and that the meat is always kept at a suitable temperature from slaughter (0-4 °C).

The effective prevention of the risk from biogenic amines from chicken meat in children's canteens requires a chain of control measures that include a careful selection of raw materials and their proper treatment until their consumption, with special attention to maintaining a suitable refrigeration temperature and storage for a limited time.

Key words

Biogenic amines, meat, histamine, tyramine, children, chicken.

Suggested citation

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1. Introduction

In 2023 and 2024, there were several foodborne outbreaks in nursery schools in Spain, associated with the consumption of chicken containing biogenic amines by children under 3 years of age.

The clinical picture appeared within a few minutes of ingestion, mainly manifesting as a localised reaction on the face (around the mouth), sometimes on the hands, with redness, rash, hives and an itching sensation. The symptoms disappeared in a short time, without the need for health care.

A strong relationship was identified between the consumption of meals containing chicken, prepared in several different ways, although, mainly, chicken thighs cut into pieces, and an immediate histaminergic reaction in those affected. No relevant risk factors were found in nursery schools that were causative or contributory to the outbreaks.

As a result of the investigations carried out of the aforementioned outbreaks, remarkable levels of biogenic amines were detected in chicken meat from different suppliers. White meats are the first to be introduced into children's diets, starting with chicken, and their consumption in schools and nurseries is frequent.

The results of the analyses of the meals prepared with chicken and on the chicken meat, both raw and frozen, indicated high concentrations of biogenic amines: histamine, cadaverine, putrescine and tyramine. The chicken meat did not exhibit any abnormal odours when being prepared.

Regarding legislation relating to biogenic amines, Regulation (EC) No. 2073/2005, on microbiological criteria applicable to foodstuffs, only sets limits for histamine in fish products (EU, 2005).

On this basis, the Scientific Committee of the Spanish Agency for Food Safety and Nutrition (AESAN) has been asked to prepare a report determining:

1. Factors that may influence the occurrence of these types of outbreaks.
2. Acceptable levels of biogenic amines in chicken meat as a whole or if there is one of them as an indicator of a level of risk for the child population under 3 years of age, as well as, where appropriate, for other vulnerable populations.
3. Aspects related to the production of chicken meat that may influence the level of biogenic amines in chicken meat and if there is knowledge of changes in production systems that may have had an influence on things like nutrition, origin of the meat, etc.
4. The influence of shelf life and storage temperature from the moment when the chickens were slaughtered.
5. In view of the above, what measures can minimise the risk in canteens that use this type of meat when the recipients are children under 3 years of age?

1.1 Biogenic amines

Biogenic amines are low molecular weight organic bases that come from the enzymatic decarboxylation of amino acids. All living organisms, including animals, plants and microorganisms, produce biogenic amines. They are involved in a wide variety of biological functions in living things. Thus, in humans, biogenic amines are involved in the control of cell division, synaptic transmission, nerve impulse transmission, immune response, or blood pressure control (del Río et al., 2024). According to their chemical structure, there are two types of biogenic amines: aliphatic amines

(putrescine and cadaverine) and aromatic amines. In turn, the latter are divided into amines with a benzene nucleus (tyramine and β -phenylethylamine) and amines with a heterocyclic nucleus (histamine and tryptamine). Based on the number of amino groups they possess, they are classified as monoamines (tyramine and β -phenylethylamine) and diamines (histamine, tryptamine, putrescine and cadaverine) (del Río et al., 2024). The polyamines spermidine and spermine have also commonly been considered biogenic amines. However, the biosynthesis and physiological functions of these are very different from those of biogenic amines and, at present, are not considered as part of these compounds. In addition, they are usually found in food in low concentrations, posing no health risks (del Río et al., 2018).

1.1.1 Histamine

Histamine is produced by decarboxylation of histidine by the enzyme histidine decarboxylase. It is the biogenic amine that is most often detected - and usually in the highest concentration - in food, especially in oily fish with high levels of histidine. In fact, its concentration is used as a food safety criterion and quality indicator in fish and products thereof. A low concentration indicates freshness of raw materials and good handling and conservation practices (Papageorgiou et al., 2018). In humans, endogenous histamine is involved in numerous physiological processes, such as gastric acid secretion, smooth muscle cell contraction, vasodilation, inflammation, or cytokine production (Ladero et al., 2010). These effects occur through interaction with receptors coupled to G proteins, which activate several signal transduction pathways, so that the final physiological effect depends on the receptor and cell type (Worm et al., 2019). Synthesized by neurons in the posterior region of the hypothalamus, histamine also acts as a neurotransmitter (Worm et al., 2019). Depending on its concentration, histamine ingested with food can increase or exacerbate these physiological processes.

1.1.2 Tyramine and β -phenylethylamine

The chemical structure of these two amines is very similar. Tyramine is produced by the decarboxylation of the amino acid tyrosine due to the action of the enzyme tyrosine decarboxylase, while β -phenylethylamine is produced by the decarboxylation of phenylalanine. In the human body, tyramine and β -phenylethylamine belong to the so-called trace compounds. These are endogenous compounds found in the body in nanomolar concentrations. Both biogenic amines share structural similarities with monoaminergic neurotransmitters such as dopamine, although their normal plasma concentration is much lower (Costa et al., 2022). The low concentration of these biogenic amines makes it difficult to determine their biological effects. Due to microbial action, tyramine can be found in high concentrations in some fermented foods and in decaying foods. This amine does not cross the blood-brain barrier, so it has no psychoactive effects.

1.1.3 Other biogenic amines

The chemical structure of cadaverine and putrescine is very similar, with five and four carbon atoms, respectively. Cadaverine is an aliphatic diamine that is synthesised from the amino acid

lysine by the action of lysine decarboxylase. Bacteria can produce putrescine from arginine by means of ornithine decarboxylase, or by deamination of agmatine (produced, in turn, from arginine by arginine decarboxylase). Tryptamine would complete the set of major amines. This is produced from the decarboxylation of tryptophan and is also a trace amine that functions as a neurotransmitter (Pei et al., 2016).

2. Producing microorganisms

Biogenic amine-producing microorganisms include a long series of Gram-positive, Gram-negative bacteria and some yeasts (Roig-Sagués et al., 2002) (Gardini et al., 2006). The ability to decarboxylate amino acids and produce biogenic amines is present in many bacteria, including species from the genera of enterobacteria (*Escherichia*, *Klebsiella*, *Citrobacter*, *Proteus*, *Shigella*, and *Salmonella*), *Micrococcaceae* (*Staphylococcus* and *Micrococcus*), lactic acid bacteria (BAL) (*Enterococcus*, the ancient genus *Lactobacillus*, *Carnobacterium*, *Pediococcus*, *Lactococcus*, and *Leuconostoc*), and pseudomonas (*Pseudomonas*) (Gardini et al., 2016) (Doeun et al., 2017) (Ekici and Omer, 2020) (Kannan et al., 2020). Different microorganisms differ in their ability to decarboxylate one or another amino acid, so each type can contribute to the formation of specific biogenic amines (Hassan et al., 2013).

The microorganisms that produce biogenic amines are also different in different foods. In fish and derived products, the predominant contaminating Gram-negative bacteria belong to species such as *Morganella morganii*, *Hafnia alvei*, *Proteus vulgaris*, *Pantoea agglomerans*, *Morganella psychrotolerans*, *Photobacterium phosphoreum* or *Enterobacter aerogenes*, among others (Emborg and Dalgaard, 2006) (Velut et al., 2019) (Hungerford, 2021). These bacteria produce mostly histamine. In poultry meat, the microorganisms frequently involved in the production of biogenic amines are enterobacteria (Lázaro et al., 2015). In fermented foods, the main microorganisms producing biogenic amines belong to the BAL species (EFSA, 2011). In these products, moreover, the presence of relatively high concentrations of two or more biogenic amines is common. Biogenic amine-producing BALs can come from raw materials, be environmental contaminants, or be part of starter or ripening cultures that are deliberately added to control fermentation. Histamine-producing BALs in fermented products belong to lactobacilli species (Díaz et al., 2016) (Ascone et al., 2017) (Wechsler et al., 2021), although bacteria producing the genera *Tetragenococcus*, *Streptococcus*, *Denococcus* and *Pediococcus* have also been described. The main producers of tyramine are bacteria of the genus *Enterococcus*, various species of lactobacilli and some of the genus *Leuconostoc*. Lastly, putrescine-producing strains have been described in a large number of BAL genera and species (Ladero et al., 2010, 2012).

3. Biochemistry and genetics of biogenic amine production

Biogenic amines are produced in the cell cytoplasm by enzymatic decarboxylation of the corresponding precursor amino acid. The amine formed and the proton resulting from decarboxylation are exchanged by means of a membrane anti-carrier with the amino acid present in the external medium (Banicod et al., 2024). This exchange helps cells control intracellular pH, particularly in acidic

environments, so the process is considered a mechanism of resistance to acid stress (Fernández de Palencia et al., 2011) (Romano et al., 2014) (Pérez et al., 2015) (del Río et al., 2016). In addition, since biogenic amines have a net positive charge more than their precursor amino acids, the exchange process leads to the displacement of positive charges out of the cells, resulting in an electrical gradient or proton-motive force that is used for nutrient transport and energy generation (Wolken et al., 2006).

Depending on the producing microorganisms, the ability to produce biogenic amines is a characteristic of a species or strain. In Gram-negative bacteria, production appears to be mostly a species characteristic. The genomes of these bacteria encode abundant decarboxylases capable of producing one or more biogenic amines. In contrast, in BAL species (e.g., *Streptococcus thermophilus*, *Lentilactobacillus parabuchneri* or *Levilactobacillus brevis*), the ability to produce biogenic amines appears to be mostly a strain-specific property (Banicod et al., 2024) (del Río et al., 2024). BAL genes involved in synthesis are frequently associated with mobile genetic elements, suggesting that they have been acquired by horizontal gene transfer (Marcobal et al., 2006) (Calles-Enríquez et al., 2010) (Romano et al., 2014). In some species of enterococci (such as *Enterococcus faecalis*, *Enterococcus faecium* and *Enterococcus durans*), however, the ability to synthesize biogenic amines is a species characteristic (Ladero et al., 2012).

4. Biogenic amines in food

Biogenic amines are present in many types of food and in noticeably different concentrations. As endogenous components, they can be found in small amounts in numerous fresh plant-based foods. The consumption of these foods does not present a health risk. Sometimes, however, some biogenic amines can reach high concentrations that can be toxic (EFSA, 2011). The highest concentrations are usually found in fish and associated products thereof, as well as in fermented beverages and foods of plant, meat and dairy origin. The accumulation of biogenic amines in food matrices is due to the presence of bacteria capable of decarboxylating free amino acids from food (Ladero et al., 2010) (Flórez-Duque et al., 2023). In general, the concentration of these amines increases as hygienic quality decreases, so the presence and levels of biogenic amines indirectly provide information on the degree of contamination and on food production, handling and storage practices. (Comas-Basté et al., 2019) (Sánchez-Pérez et al., 2021).

The biogenic amine detected most frequently and in the highest concentration in fish and products thereof is histamine, mainly in oily fish with high levels of histidine. Fish and fresh fish products normally do not contain histamine or only low levels. This amine is mainly produced by the action of contaminating Gram-negative bacteria and is indicative of deterioration, related to deficiencies in the cold chain (Papageorgiou et al., 2018) (Hungerford, 2021). When freshness is lost, in addition to histamine, other amines related to the decarboxylase activity of Gram-negative bacteria such as cadaverine and putrescine frequently accumulate (Comas-Basté et al., 2019). The situation is more complex in fermented foods in which the biosynthesis of biogenic amines is mainly due to the action of Gram-positive BAL, also responsible for the fermentation and organoleptic characteristics of the final product (Ladero et al., 2017). In these products, the most abundant biogenic amines are

tyramine, histamine, and putrescine, followed by cadaverine and β -phenylethylamine (EFSA, 2011). Fermented foods present optimal conditions for the accumulation of biogenic amines due to a diverse microbiota and the intense proteolysis that takes place during maturation, which ensures the availability of precursor amino acids (Linares et al., 2012) (Wójcik et al., 2023).

With the exception of putrescine and cadaverine, the vast majority of biogenic amines do not cause sensory modifications in food and, therefore, their presence is not easily detected (Schirone et al., 2022). In addition, they are thermostable, so they are not inactivated during usual food processing operations, including cooking (Gardini et al., 2016) (Liu et al., 2024). Therefore, the safest way to reduce the risk of its consumption is to reduce its formation as much as possible.

4.1 Biogenic amines in meat and meat products

Meat and meat products are a group of foods that, due to their high protein content and the high probability of microbial contamination during slaughter and processing, engender the formation of biogenic amines that can appear in a wide range of concentrations. Fresh meat usually has spermine and spermidine concentrations of 20-60 mg/kg and <10 mg/kg, respectively, and low concentrations of other biogenic amines. However, prolonged storage or unsuitable storage conditions can trigger microbial development and the production of large amounts of biogenic amines, with a predominance of tyramine, cadaverine, putrescine and histamine (Triki et al., 2018) (Ruiz-Capillas and Herrero, 2019) (Durak-Dados et al., 2020) (Dabadé et al., 2021). These amines can appear in a wide range of concentrations in different types of meat and meat-derived products (Jairath et al., 2015) (Schirone et al., 2022). A high concentration of one or more biogenic amines suggests high microbial growth and, with it, poor food quality. Thus, levels of cadaverine and putrescine have been proposed as indicators of deterioration of beef and poultry meat during storage (Vinci and Antonelli, 2002). Raw pork is considered deteriorated with cadaverine and putrescine levels above 15 mg/kg (Siripongpreda et al., 2020). In cured meat products the predominant amine is tyramine (Schirone et al., 2022). In contrast to the values of individual biogenic amines, some authors have proposed a Biogenic Amines Index (BIA) as an indicator of meat quality. This index corresponds to the sum of the values of tyramine, cadaverine, putrescine and histamine (Durak-Dados et al., 2020). The BIA enables differentiation between fresh meat (BIA <5 mg/kg), acceptable meat (BIA between 5 and 20 mg/kg), low quality meat (BIA between 20 and 50 mg/kg) and spoiled meat (BIA >50 mg/kg). Since the final concentration of biogenic amines in meat products varies depending on many handling and processing factors, the BIA value is more useful as an indicator of the quality of fresh meat than of matured or heat-treated products (Durak-Dados et al., 2020).

4.1.1 Biogenic amines in chicken meat

In general, poultry meat has a high risk of contamination during slaughter and processing, which gives rise to the formation of biogenic amines, even under refrigerated conditions. Chicken meat in particular is especially sensitive to the formation of biogenic amines due to its muscle fibres being particularly susceptible to proteolysis. The high water activity (a_w) and the availability of nutrients

make this meat an ideal culture medium for a large number of microorganisms. In chicken meat, the microbial group most frequently involved in the production of biogenic amines is that of enterobacteria (Lázaro et al., 2015). Biogenic amines can be produced during the handling, storage and distribution of meat, which means that the degree of initial contamination and environmental conditions during processing can significantly influence the types of biogenic amines and their concentration (Saewa et al., 2021) (Alessandrini et al., 2022). Although there are significant differences between samples from different studies, in general, the most common biogenic amines in chicken meat are, in this order, histamine, tyramine, cadaverine, putrescine, phenylethylenediamine, spermine and spermidine (Wójcik et al., 2022). The content of histamine, tyramine, cadaverine and putrescine in different pieces of fresh chicken meat and its derived products preserved at low temperature over time is shown in Table 1. The levels of biogenic amines in the fresh starting pieces vary significantly between the different studies, which suggests variability in the quality of the raw material (Wójcik et al., 2022). In several studies, starting with chicken meat with a low concentration of biogenic amines, after storage of 6-8 days at 4 °C, appreciable levels of the most toxic biogenic amines, histamine and tyramine, can be detected (Table 1). This suggests that low-temperature storage for a shorter time could be effective in decreasing the toxic levels of biogenic amines in chicken meat. Although not listed in the table, the concentration of most biogenic amines increases remarkably when analyses are carried out on samples preserved for a longer time (9-12 days).

5. Biogenic amines and toxicity

The total content of biogenic amines in the body is the sum of the endogenous biogenic amines that are produced in human cells and those that are incorporated exogenously. These come mostly from food, but can also be synthesized in the gut by microbiota. Due to its physiological effects, the concentration of biogenic amines in cells and tissues is tightly regulated (Linsalata and Russo, 2008). Under normal conditions, exogenous biogenic amines are rapidly metabolised in the intestinal mucosa, resulting in physiologically under-active compounds. Oxidation is the main catabolic pathway of biogenic amines, although acetylation and methylation may also be involved (Hungerford, 2021).

Depending on the amino groups, the oxidation reactions of biogenic amines are catalysed by specific monoamino- or diamino-oxidases (MAO or DAO, respectively) (Álvarez and Moreno-Arriivas, 2014).

Biogenic amines ingested with food can interact with specific receptors and induce digestive, circulatory and respiratory disorders (Linsalata and Russo, 2008). The severity of symptoms depends on the amount and variety of biogenic amines ingested and the susceptibility of the individual, which in turn depends on the activity of the MAO and DAO enzymes. The consumption of high concentrations of biogenic amines can cause saturation of detoxifying enzymes (Maintz and Novak, 2007). The activity of these may also be reduced by genetic causes or by the presence of inhibitors, such as isoflavones, some of their metabolites, nicotine, or MAO inhibitor drugs (MAOIs) (Hutchins et al., 2005) (Sved et al., 2022) (Van den Eynde et al., 2022). In certain cases, the presence of inhibitors causes the intake of biogenic amines in low concentrations to have serious toxic effects

(Blackwell, 1963). Likewise, concomitant consumption with alcohol can potentiate the toxic effect of biogenic amines by increasing the permeability of the intestinal wall (Wöhrl et al., 2004).

The main acute toxicity effects, which can appear rapidly after a specific intake of biogenic amines, are scombroidosis, in the case of histamine, and hypertensive crises, in the case of tyramine in cheese consumers treated with MAO inhibitors. On the other hand, chronic exposure to certain amines could induce carcinogenic processes, since compounds such as putrescine and cadaverine can react with nitrites to form nitrosamines, substances with recognized carcinogenic potential (Jaguey-Hernández et al., 2021). Establishing the degree of toxicity of biogenic amines is difficult because it depends on the efficiency of the detoxification process in the intestinal tract and the presence and concentration of other biogenic amines in the body (Ekici and Omer, 2020). The toxicity of biogenic amines is varied, although histamine and tyramine are undoubtedly the most toxic. The European Food Safety Authority (EFSA) has not established No Observed Adverse Effect Levels (NOAELs) for these biogenic amines, but suggests that healthy adults could consume between 25 and 50 mg of histamine and 600 mg of tyramine per meal without presenting adverse effects (EFSA, 2011).

Many authors acknowledge the absence of experimental data on the toxicity of biogenic amines. This absence of experimental data is usually corrected by applying uncertainty factors. These are safety values used in the risk assessment to calculate the reference dose that is considered safe or below which an adverse effect is unlikely to occur (IGHRC, 2003). The value of the safety factors depends on the toxic effect, the size and type of the population to be protected, and the quality of the available toxicological and exposure data. In the 1950s, a universal uncertainty factor of 100 was established, called the "safety margin" (Dankovic et al., 2015). This factor can be broken down into various specific uncertainty factors that involve the extension of animal experimentation data to humans, the lack or insufficiency of data, intraspecific sensitivity, the extension of short-term experimental effects to long-term exposure, etc. These specific factors have variable values depending on how they are calculated. In general, each is usually given a value of 10 (Dankovic et al., 2015) (Johanson et al., 2023).

Table 1. Average biogenic amine content (mg/kg) in various pieces of fresh chicken meat and products thereof. Effect of storage temperature in air cooling for various periods of time on the formation of biogenic amines

Chicken part	Storage conditions	Histamine		Tyramine		Tryptamine		Putrescine		Cadaverine		Reference
		Fresh	Preserved	Fresh	Preserved	Fresh	Preserved	Fresh	Preserved	Fresh	Preserved	
Filletts (n=24) *	3.5 °C, 7 days	0.38	1.35	1.65	42.65	n.d.	n.d.	1.30	14.64	1.79	49.03	Chmiel et al. (2022)
Thighs (n=9) *	4 °C, 6 days	-	-	-	-	-	-	12.06	22.44	8.69	80.29	Min et al. (2023)
Breast (n=9) *		-	-	12.16	-	-	-	9.32	11.62	33.03	50.65	
Chicken preparations (n=4)	-	245.8	n.d.	262.25	n.d.	n.d.	n.d.	3534.20	n.d.	392.32	n.d.	Czajkowska-Mysiek and Leszczyńska (2017)
Chicken meat (n=4)	4 °C, 4 days	23.1	n.d.	5.55	n.d.	21.9	n.d.	28.25	n.d.	12.77	n.d.	Yue et al. (2023)
Breast (n=3)	4 °C, 4 days	-	10.8	-	5.48	-	15.30	-	27.01	-	27.40	Jastrzebska et al. (2024)
Chicken pieces (n=36) *	4 °C, 7 days	-	4.9	-	23.9	n.d.	n.d.	-	-	-	-	Esposito et al. (2022)
Frozen breast (n=39)	4 °C, 6 days	3.35	6.04	0.42	2.74	n.d.	n.d.	0.32	15.68	0.01	67.10	Lázaro et al. (2014)
Breast (n=3) *	4 °C, 8 days	-	-	0.2	2.3	n.d.	n.d.	58.3	182.4	19.8	43.1	Balamatsia et al. (2006)
Breast (n=5) *	4 °C, 6 days	0.18	0.24	-	-	-	-	0.28	0.80	1.65	3.59	Lázaro et al. (2019)
Breast (n=16) *	4 °C, 4 days	-	-	-	-	n.d.	n.d.	-	-	-	-	
Thighs (n=16) *		0.7	0.5	-	2.1	n.d.	n.d.	-	-	-	-	
Sausages (n=10)		0.9	n.d.	0.1	n.d.	-	-	0.6	-	0.4	-	Silva and Glória (2002)
Mortadella (n=10)		1.5	n.d.	0.2	n.d.	-	n.d.	2.6	n.d.	0.6	n.d.	
Cured (n=10)		13.5	n.d.	7.4	n.d.	5.7	n.d.	15.1	n.d.	8.0	n.d.	
Meatballs (n=10)		-	n.d.	0.3	n.d.	-	n.d.	0.6	n.d.	0.2	n.d.	
Hamburgers (n=10)		0.2	n.d.	0.5	n.d.	-	n.d.	0.6	n.d.	0.7	n.d.	
Nuggets (n=10)		-	n.d.	-	n.d.	-	n.d.	-	n.d.	-	n.d.	
Minced breast (n=9) *	4 °C, 6 days	1.61	4.41	-	3.14	n.d.	n.d.	1.02	1.17	-	8.9	Wojnowski et al. (2018)
Minced breast (n=3) *	4 °C, 6 days	1.47	3.80	-	4.15	n.d.	n.d.	0.99	1.82	-	10.47	Wojnowski et al. (2019)

n.d.= not detected. * Days of conservation after slaughter, precisely specified.

5.1 Histamine toxicity

Histamine poisoning is known as scombroid poisoning due to its association with the consumption of oily fish of the *Scombridae* and *Scorpaenidae* families with high histidine content, such as tuna, mackerel, bonito, etc. These fish are responsible for 98 % of histamine poisonings (Nuñez and Calzada, 2016) (Colombo et al., 2018). Of the non-scombroid species, lemonfish (*Amberjack*), *el dorado* (*Mahi-mahi*), sardines, yellowtail snappers and herring are also responsible for poisoning by this biogenic amine (Demoncheaux et al., 2012) (Harmelin et al., 2018). The symptoms of histamine poisoning are closely related to its physiological functions and affect the skin (redness, rash, hives, itching, oedema, or local inflammation), the gastrointestinal tract (nausea, vomiting, and diarrhoea), and the circulatory and nervous systems (hypotension, headache, dizziness, palpitations, breathing difficulties, and tingling) (EFSA, 2011) (Ekici and Omer, 2020) (Tabanelli, 2020). The effects can be severe in individuals who, for genetic or pharmacological reasons, are deficient in DAO (diamine oxidase) (Bodmer et al., 1999). From 2020 to the present, the European RASFF (Rapid Alert System for Food and Feed) reported 143 alerts for the excessive presence of biogenic amines in food in the European Union, of which 141 were histamine (RASFF, 20205). In Spain, in 2020, four outbreaks of histamine poisoning were reported (AESAN, 2022). However, the symptomatic similarity between food allergy and histamine poisoning suggests that the latter may be under-diagnosed.

In human intestinal epithelial cell lines, histamine concentrations equivalent to a dose greater than 440 mg/kg have been shown to be cytotoxic (Linares et al., 2016). Such concentrations are easily reached in certain fish, products thereof and cheese. The mechanism of cytotoxicity of this biogenic amine is the induction of apoptosis (Linares et al., 2016). In response to allergic reactions or tissue damage, histamine is also released from mast cells (white blood cells). The proximity of mast cells to blood vessels, coupled with the potent actions of histamine, suggests that this amine may influence cerebral blood flow (Purves et al., 2001).

Several authors have described considerable inter-individual variability in histamine tolerance. In general, the intake of 50 mg of this biogenic amine does not cause symptoms in healthy adults (Wöhrl et al., 2004), while 75 mg of pure oral liquid histamine causes mild symptoms in half of adults without a history of intolerance (Wöhrl et al., 2004) (Rauscher-Gabernig et al., 2009).

5.2 Tyramine toxicity

Tyramine is found in large amounts in some cheeses due to the metabolism of tyraminogenic lactic bacteria (Linares et al., 2011). Tyramine poisoning causes the so-called “cheese reaction”. This biogenic amine can also be present in high concentrations in meat and meat products, mainly those that have been fermented (Tabanelli, 2020). Tyramine poisonings, however, are rare. The RASFF system has only reported one tyramine alert in the last 20 years (associated with a *Gruyère* cheese made with raw milk) (Ref. 2022.6393) (RASFF, 2025).

When tyramine is ingested, it reaches the intestine and is detoxified by MAO. If the amount ingested is too high, or MAO activity is inhibited, excess tyramine reaches the bloodstream, causing vasoconstriction. Tyramine can also be hydroxylated within the sympathetic nerve endings forming octopamine, which displaces noradrenaline from the storage vesicles. Part of the released noradre-

naline interacts with TAAR (Trace Amine Associated Receptors) causing hypertension. Noradrenaline and octopamine also affect the transmission of nerve impulse at the endings of the sympathetic nervous system, which may cause nausea, vomiting, or headaches (Ladero et al., 2010) (Andersen et al., 2019). Tyramine is capable of raising systolic blood pressure and causing cardiac crises or cerebral haemorrhage (Blackwell, 1963). Oral administration of 125 mg tyramine exerts effects on blood pressure in healthy people, and a dose of 500 mg increases baseline systolic pressure by at least 30 mm (Van den Berg et al., 2003). Currently, there is insufficient information to establish the NOAEL of tyramine in humans (EFSA, 2011).

5.3 Toxicity of other biogenic amines

Little information is available about the toxicity of other biogenic amines, although they are all known to produce a variety of harmful health effects, and have been linked to multiple outbreaks of foodborne disease (Omer et al., 2021). Apart from histamine and tyramine, the most common biogenic amines in food are putrescine, cadaverine, β -phenylethylamine, tryptamine, spermine and spermidine (Ekici and Omer, 2018).

Although no human dose-response studies have been conducted to determine its adverse effects, the toxic effects of putrescine and cadaverine are considered less potent than those of histamine and tyramine. Putrescine ingestion has been associated with hypotension, bradycardia, and limb paralysis (Shalaby, 1996). Digestive exposure to cadaverine has been associated with effects similar to those of putrescine (Shalaby, 1996). In subacute oral toxicity trials in rats, a NOAEL for putrescine and cadaverine of 180 mg/kg b.w./day has been determined (Til et al., 1997). β -phenylethylamine and tryptamine, on the other hand, act as neuromodulators or neurotransmitters, and, like tyramine, cause vasoconstriction, which can produce hypertension (Tittarelli et al., 2015).

Histamine and tyramine also appear to have synergistic cytotoxic effects (del Río et al., 2017), which may be relevant as both are often present in the same food. Synergistic effects may also occur among other combinations of biogenic amines. Thus, putrescine, cadaverine and phenylethylamine seem to increase the adverse effects of histamine (Omer et al., 2021). The polyamines putrescine, cadaverine, spermine and spermidine do not themselves have toxic effects, but they are capable of inhibiting the enzymes that detoxify histamine and tyramine, so they could potentiate the toxic reactions caused by these (Lehane and Olley, 2000) (Karovičová and Kohajdová, 2005).

5.4 Toxicity in sensitive persons

Two states are recognised regarding the toxicity of biogenic amines: intoxication and intolerance. In the case of histamine, intolerance is defined as a disorder with a wide range of non-specific gastro- and extra-intestinal symptoms that derive from the poor degradation of the amine in the intestine (EFSA, 2011). It is estimated that histamine intolerance affects up to 3 % of the world's population, with a higher incidence in women than in men (in a 4:1 ratio) (Jarisch, 2014). Sensitive individuals should follow a low histamine diet and, in some cases, use an exogenous DAO supplement, as for them there are no safe histamine levels (Sánchez-Pérez et al., 2022). In patients with intolerance, ingestion of small amounts of histamine can cause severe toxic effects (EFSA, 2011).

Tyramine, on the other hand, is very toxic in people being treated with MAOIs. Ingested together with these, 6 mg of pure tyramine will have extremely toxic effects (McCabe-Sellers et al., 2006). New generation MAOIs (reversible inhibitors) do not induce such a high sensitivity and allow a higher tolerance (between 50 and 150 mg) (McCabe-Sellers et al., 2006).

Although there are very little data available, other biogenic amines, such as spermine and spermidine, have been linked to food allergies (Kalac & Krausová, 2005).

5.5 Toxicity in children

Although there are no data available on toxicity in children, a greater sensitivity of this population to biogenic amines is expected, since they have immature enzyme systems (such as DAO) and, therefore, a lower detoxification capacity. Due to their low weight, small doses of biogenic amines may cause more pronounced effects compared to those in adults (Rosell-Camps et al., 2013). Children are therefore one of the populations most vulnerable to the presence of biogenic amines in the food they eat.

6. Regulation of the presence of biogenic amines in food

European regulations establish maximum limits of 200 mg/kg for histamine in fish from species with a high content of free histidine in muscle tissue, and 400 mg/kg for products derived from these fish with enzymatic maturation in brine (category 1.27 a) (Regulation (EC) No. 2073/2005 and subsequent modifications: 144/2007, 365/2010) (EU, 2005). The legislation applies to certain fish species of the families *Scombridae*, *Clupeidae*, *Eugraulidae*, *Coryphenidae*, *Pomatomidae* and *Scomberesocidae* throughout their shelf life with a sampling plan comprising nine units ($n=9$), two of which (tolerance; $c=2$) may have a concentration between 100 (m) and 200 (M) mg/kg of histamine and none should be above the maximum limit. Likewise, the Regulation also covers the levels of histamine in the processed products of these species, with a similar sampling plan of nine units, two of which can have between 200 and 400 mg/kg of histamine and none exceed the maximum limit.

No standards or guidelines have been published regarding the content of biogenic amines in meat, meat products or other types of food (Schirone et al., 2022) (del Río et al., 2024).

In the United States, the FDA (Food and Drug Administration) has set a maximum histamine concentration of 50 mg/kg for food in general (FDA, 2022), a much more restrictive limit than that of current European legislation. An acceptable histamine level of 100 mg/kg in the muscles of species of the families *Scombridae*, *Coryphaenidae*, *Scomberesocidae*, *Pomatomidae* and *Clupeidae* has been established by the MERCOSUR Resolution and Technical Regulation on Identity and Quality of Fresh Fish (whole and gutted) (Rodríguez et al., 2014). The Nutritional Code of the Slovak Republic sets an upper limit for two biogenic amines: histamine (20 mg/kg in beer and 200 mg/kg in fish and products thereof) and tyramine (200 mg/kg in cheese). The Dairy Research Institute of the Netherlands and the Czech Republic have foreseen a recommended upper limit of 100-200 mg/kg for histamine in meat products. There are no established standards or criteria for cadaverine, putrescine and other biogenic amines, although some recommendations have been suggested (Shashank et al., 2021).

7. Control and prevention of biogenic amine formation

The importance of preventing the excessive accumulation of biogenic amines in food is related to their toxicity and the impact they have on human health. This is also related to its influence on quality, as some biogenic amines give rise to strange flavours or aromas. Biogenic amines are produced under two simultaneous conditions: the presence of the precursor amino acids and microorganisms with specific amino acid decarboxylases. Microorganisms with these activities can come from raw materials or be contaminants that access food during processing or storage (Papageorgiou et al., 2018). The presence of toxic levels of biogenic amines is associated with a high concentration ($>7 \log_{10}$ CFU/g) of decarboxylating microorganisms. Thus, biogenic amine content can be used as an indirect indicator of microbial load (Gardini et al., 2016). Since, once produced, biogenic amines are difficult to eliminate, strategies to prevent their accumulation in food are focused on reducing their formation, which leads to the reduction of the development of producing microorganisms.

Other factors that influence the presence of biogenic amines in food are the composition of the food, handling and processing practices (for example, fermentation, maturation, addition of additives or processes that influence contamination after treatment), the final pH of the product and storage conditions (time, temperature and composition of the atmosphere) (Ruiz-Capillas and Herrero, 2019) (Dabadé et al., 2021). The strategies included in the scientific literature for reducing biogenic amine content in foods include the use of top quality raw materials and the use of appropriate processing methods, the use of selected starter cultures for the production of fermented products, the addition of preservatives or natural antimicrobial extracts, and the treatment of foods with emerging experimental conservation technologies (some unauthorized or whose use is only allowed in the processing of certain foods or food additives) such as High Hydrostatic Pressures (HPAs), irradiation or packaging in Modified Atmospheres (MAs). These methods make it possible to reduce the content of biogenic amines by inhibiting the development of producing bacteria or reducing the activity of decarboxylases.

7.1 Origin and characteristics of meat

Several studies show that the origin of meat can influence the formation of biogenic amines. Thus, the formation of histamine and tyramine tends to be lower in packaged meat products made exclusively from pork (such as cooked ham and cured ham) (Wortberg and Woller, 1982) (Vidal-Carou et al., 1990) than in those containing mixtures of beef and pork (salami, sausage, chorizo or Bologna sausages) (Jairath et al., 2015). On the other hand, under the same storage conditions, the biogenic amine content in chicken meat is generally higher than in beef or pork due to its structure and protein composition (Alessandrini et al., 2022). The fat content of meat also seems to influence the formation of biogenic amines, as this is negatively correlated with the a_w . A low a_w inhibits microbial growth and reduces proteolysis (Liu et al., 2024), factors that directly affect the production of biogenic amines.

7.2 Use of non-amine producing starter cultures

Europe is the largest producer and consumer of fermented meat products, which are the foods with the highest level and diversity of biogenic amines. Fermentation of meat increases the acidity of the

raw material, which, together with dehydration, the addition of sodium chloride, and the presence of microorganisms, encourages proteolysis and the appearance of free amino acids that constitute the substrate of decarboxylases (Jairath et al., 2015) (Ruiz-Capillas and Herrero, 2019). The best strategy to reduce the concentration of biogenic amines in these products is to use selected starter cultures that do not produce them. The starter cultures compete with native and contaminating bacteria with decarboxylase activity, thereby reducing the formation of biogenic amines (Nieto-Arribas et al., 2009). They also favour a rapid decrease in pH, which contributes to inhibiting many producing microorganisms (Domínguez et al., 2016) (Gardini et al., 2002) (González-Fernández et al., 2003). Some starter cultures without decarboxylase activity have enzymes that oxidise or degrade biogenic amines generating aldehydes, H_2O_2 and ammonia, thereby reducing their concentration in fermented products (La Gioia et al., 2011) (Zaman et al., 2011) (Cueva et al., 2012) (Naila et al., 2024).

7.3 Technological processing methods

In addition to the intrinsic properties, the treatment and technological processes to which food is subjected also influence the generation of biogenic amines. Thus, mechanical damage to meat results in an increase in proteolysis and the release of free amino acids, which facilitates the formation of biogenic amines (Cruz-Monterrosa et al., 2017). Other treatments have the effect of reducing the formation of biogenic amines. Smoking ham, for example, reduces its concentration of biogenic amines, as it inhibits microbial growth, reduces a_w and partially inhibits proteolysis (Schirone et al., 2022). The addition of salt in the processing of many meat products also has a great influence on the reduction of biogenic amines, as it inhibits microbial growth and reduces decarboxylase activity (Roseiro et al., 2006) (Gardini et al., 2008, 2016) (Bover-Cid et al., 2009). In this sense, Gram-negative bacteria are, in general, more sensitive to the increase in salt concentration than Gram-positive bacteria (Keব্য et al., 1999). Some authors, however, attribute to salt a potentiation of the metabolic activity of decarboxylating microorganisms, indicating, in particular, the role of sodium ions in the Na/H^+ exchanger that is responsible for expelling protons to the outside of the cell (Lorencová et al., 2014) (Gardini et al., 2016).

7.4 High hydrostatic pressures

High Hydrostatic Pressures (HHPs) are an emerging technology that involves applying pressures of varying intensity to food (up to 600 MPa) in order to reduce the microbial load and thereby extend its shelf life and improve its safety and quality. The efficacy of HHP varies significantly depending on the type of food and the specific treatment conditions, which requires optimising the conditions for each particular application (Novella-Rodriguez et al., 2002) (Doeun et al., 2016). HHP is being tested as a promising alternative to traditional heat treatments for meat preservation, although it can influence physical and sensory properties such as hardness, colour, and juiciness. Thus, the application of a pressure of 500 MP in dry and semi-dry fermented sausages improved microbial quality and reduced the formation of biogenic amines during storage (Latorre-Moratalla et al., 2007), without causing significant changes in organoleptic quality. Similar results have been obtained for fermented sausages made of chicken, pork and beef (Simon-Sarkadi et al., 2012) (Borges et al.,

2020). In most cases, the application of HHP shows a reducing effect on the formation of putrescine and cadaverine, while increasing the formation of tyramine and spermidine. Tyramine is mainly related to the activity of fermentative BALs, while putrescine and cadaverine generally derive from the action of non-fermenting bacteria. The reduction in biogenic amines is mitigated by the reduction in producer populations that can be BAL, enterococci or enterobacteria (Latorre-Moratalla et al., 2007) (Espinosa-Pesqueira et al., 2018). HHPs can also reduce proteolytic activity, resulting, again, in reduced biogenic amine formation (Espinosa-Pesqueira et al., 2018).

7.5 Packaging in modified atmospheres

Packaging in Modified Atmospheres (MAs) is a technique widely used in the food industry to reduce microbial proliferation in food. Mixtures of gases such as carbon dioxide (CO₂) and nitrogen (N₂) limit the proliferation of aerobic microorganisms. This method has been successfully employed for storage of meat and meat products, prolonging their quality and shelf life (Fraqueza et al., 2012) (Doeun et al., 2017). MAs with high oxygen concentration prevent the accumulation of putrescine and cadaverine in chicken breast (Chmiel et al., 2022) better than vacuum or air packaging. In this same study, the importance of good storage conditions was also pointed out, with better product stability in low temperature and humidity conditions being observed. Increasing the concentration of CO₂ in cooked chicken containers reduces the formation of putrescine and cadaverine (Gallas et al., 2010) (Rodríguez et al., 2015). MAs have also demonstrated a reducing effect on the formation of biogenic amines in fresh chorizo stored in atmospheres with CO₂ and N₂ or argon (Ruiz-Capillas et al., 2012) (González-Tenorio et al., 2013).

7.6 Use of natural antimicrobial extracts

Plant extracts, such as rosemary, thyme or oregano, among others, possess antimicrobial properties effective in reducing the microbial load and, consequently, could limit the production of biogenic amines. These products are attractive to consumers due to their natural origin and are perceived as having less chemical risk, compared to that of synthetic preservatives (Wójcik et al., 2022). There are numerous experimental trials on the effect of various plant extracts on the formation of biogenic amines (Houicher et al., 2015) (Kongkiattikajorn, 2015) (Sun et al., 2018) (Burgut, 2020) (Özoğul et al., 2021) (Li et al., 2023) (Kuley et al., 2024).

However, in order for these types of extracts to be used as preservatives, they must be authorised and must comply with the legislation governing food additives: Regulation (EC) No. 1333/2008 (EU, 2008), on food additives, and Regulation (EU) No. 231/2012 (EU, 2012), establishing specifications for additives that are reflected in Annexes II and III of Regulation (EC) No. 1333/2008.

7.7 Controlling environmental factors

The formation of biogenic amines in food is related to the environmental conditions that allow the development and activity of the decarboxylating bacteria in its microbiota. Strict control of factors such as temperature, pH and humidity is crucial to reduce or completely inhibit the formation of biogenic amines.

7.7.1 Temperature

The storage and processing temperature is one of the most important parameters for the reduction of biogenic amines in many foods. Freezing inhibits microbial growth and, consequently, the production of biogenic amines. However, the optimal temperature range for the production of biogenic amines by mesophilic bacteria is 20 to 37 °C (EFSA, 2011). These elevated temperatures accelerate the growth of microorganisms that decarboxylate amino acids, drive protein catabolism, and increase decarboxylase activity, leading to the production of biogenic amines. In fish, the optimal temperature for histamine production by *Morganella morganii* is 25 °C (Latorre-Moratalla et al., 2012). Tyramine production in minced meat by *Carnobacterium divergens* is higher at 25 than at 15 °C (Masson et al., 1999). Similarly, Xiao et al. (2010) showed that the levels of putrescine, tyramine, and cadaverine in Edam cheese matured at 10 °C were higher than those produced at 5 °C. To minimize the multiplication of microorganisms and the concomitant production of biogenic amines, perishable products should be kept at temperatures between 0 and 4 °C (Buňková et al., 2010), throughout the production and processing chain until the time of consumption. In this regard, in order to minimize the formation of histamine, the FDA recommends preserving fish at a temperature below 4.4 °C (FDA, 2011).

7.7.2 pH and a_w

pH is a factor that has a major influence on bacterial growth, decarboxylase activity, and the bacterial response to acid stress (Barbieri et al., 2019). The optimal pH value for the formation of biogenic amines depends on the microorganism and the amine under consideration. Some authors have found optimal pH values of 4.5 (Tabanelli et al., 2012), 5.0 (Moreno-Arribas and Louvand-Funel, 2001) (Zhang and Ni, 2014), between 5.0 and 6.0 (Bargossi et al., 2015), or between 5.5 and 6 (Greif et al., 2006) (Liu et al., 2014). However, in other studies, higher optimal pH values (7.0) have been observed, especially when Gram-negative bacteria are involved (Kanki et al., 2007). Decarboxylation contributes to increased pH (both intra- and extra-cellular) and can provide supplemental energy to cells (Gardini et al., 2016). In acid-sensitive bacteria, the addition of organic acids to foods, or correct acidification of fermented products, can reduce the development of many microbial biotypes and, concomitantly, reduce the synthesis of biogenic amines (Ruiz-Capillas and Herrero, 2019). The decrease in the a_w of a food has similar effects, since it also reduces the growth of the producing microorganisms (Kebary et al., 1999).

7.8 Storage time

After temperature, storage time is a critical parameter in the formation of biogenic amines, as it supports the proteolysis of proteins into peptides and their subsequent degradation to oligopeptides and free amino acids (Durak-Dados et al., 2020). The relationship between storage time and biogenic amine accumulation has been demonstrated in various meat and meat product samples (Halász et al., 1994) (Krizek et al., 2002) (Marcobal et al., 2006). Prolonged storage induces the production of biogenic amines even in frozen meat. Thus, for example, the average concentration of putrescine and cadaverine increased from 0 to 1121.48 µg/g in different cuts of beef after 5 months of storage at -18 °C (Motaghifar et al., 2021).

7.9 Analysis and monitoring of biogenic amines in food

Monitoring the concentration of biogenic amines in food during production and storage is a measure of great interest to ensure food safety. Constant monitoring helps to detect products that exceed the established safety limits and allows evaluation of the effectiveness of prevention strategies implemented in the production chain (EFSA, 2011).

7.10 Good hygiene practices

Raw materials must be of high microbiological quality and handled under strict hygienic conditions. Control of the initial microbial load is key, as microorganisms responsible for the production of biogenic amines, such as certain species of enterobacteria and pseudomonas, are usually introduced at early stages of processing, and then proliferate if appropriate measures are not taken (Sivamaruthi et al., 2021) (Schirone et al., 2022).

Compliance with good hygiene and manufacturing practices by operators is also a basic requirement. Thus, Regulation (EC) No. 852/2004 (EU, 2004a) establishes the general hygiene requirements for all food businesses at all stages of the food chain, from primary production to the final consumer. Likewise, Regulation (EC) No. 853/2004 (EU, 2004b) lays down specific hygiene rules for food of animal origin, such as meat, fish and dairy products, complementing Regulation (EC) No. 852/2004, especially in post-primary production phases.

8. Exposure to biogenic amines and risk

8.1 Consumption of meat from chickens

It is estimated that in 2018 global production of chicken meat in the world reached 119.7 million tons (Wójcik et al., 2022). Chicken meat stands out for its high nutritional quality, offering, at the same time, low levels of fat and cholesterol (Esposito et al., 2022). The consumption of this food has grown significantly in recent decades, due, among other factors, to its low production cost and the absence of cultural restrictions on its consumption (Wójcik et al., 2022). Chicken meat consumption is projected to continue to increase, reaching 15.1 kg per capita globally and 33 kg per person in the European Union by 2029 (Saewa et al., 2021).

8.2 Consumption of meat from chickens by children

Chicken meat provides children with easily digestible protein and essential nutrients such as iron, calcium and B vitamins (Esposito et al., 2022). Table 2 shows the consumption data of chicken meat in Spain by age of different population groups. The mean consumption per child between 0 and 3 years is around 2.7 g/kg b.w./day for children aged 3-11 months and 2.3 mg/kg b.w./day for children aged 12-35 months.

Table 2. Chicken meat consumption in Spain by age of population groups

Population group	Consumption (g/kg b.w./day) ^a					
	Children	Children	Children	Teenagers	Adults	Older adults
Age range	3-12 months	12-35 months	3-10 years	10-17 years	18-64 years	≥65 years
Mean	2.74	2.30	1.65	0.88	0.48	0.31
95th percentile	8.50	7.45	5.90	3.15	1.71	1.29

^a Data taken from the EFSA Comprehensive Food Consumption Database (EFSA, 2025). Based on ENALIA (child and adolescent population) and ENALIA2 (adult population) surveys.

8.3 Risk of chicken consumption in children

In fresh chicken meat and freshly-prepared chicken meat dishes biogenic amine concentrations are low (Table 1) and their consumption should not pose a significant health risk to children. However, improper conservation can promote the accumulation of biogenic amines, increasing the chances of poisoning. Beyond the limits set for histamine in Regulation (EC) No. 2073/2005 (EU, 2005), there is no specific regulation on the content of biogenic amines in foods intended for the infant population.

8.4 Toxic risk assessment of the presence of biogenic amines in chicken meat

It should be noted that EFSA has not established Tolerable Daily Intakes (TDI) for biogenic amines in humans, nor is there a proposal for Acute Reference Dose (ARfD) values for adults or children. Only potential ARfD values per healthy adult and food have been proposed and will be used as a reference. These values are 50 mg histamine and 600 mg tyramine (if no MAOIs are taken) (Turna et al., 2024). For the remaining biogenic amines, no reference values have been put forward.

The ARfDs are proposed for adults, so to calculate the risk in children under 3 years of age, subject of this assessment, the reference values are adjusted to this specific population. If the average weight of an adult is set at 70 kg, ARfDs will be calculated for the average weight (5 kg) of a child aged 0-1 years and for the average weight (12 kg) of a child aged 1-3 years (EFSA, 2012):

$$ARfD (children) = \frac{ARfD \text{ adults}}{\text{Standard adult weight}} \times \text{child weight}$$

- Adult ARfD Histamine= 50 mg (0.81 mg/kg) → 3.57 mg in children aged 0-1 years.
- Adult ARfD Tyramine= 600 mg (8.57 mg/kg) → 42.86 mg in children aged 0-1 years.
- Adult ARfD Histamine= 50 mg (0.81 mg/kg) → 8.57 mg in children aged 1-3 years.
- Adult ARfD Tyramine= 600 mg (8.57 mg/kg) → 102.85 mg in children aged 1-3 years.

Table 3 presents the adjusted concentrations of biogenic amines with ARfD in the samples analysed in relation to the outbreaks in school canteens mentioned in the introduction of this report in children aged 0-1 years, as well as the percentage (%) of contribution to the histamine and tyramine ARfDs when consuming a 40 g portion of food (FNS, 2018) (EFSA, 2025).

Table 3. Adjusted concentrations of BAs with ARfD in the samples analysed in school canteens						
Food	ARfD histamine children (mg)	Histamine (mg/kg)	% of contribution in 40 g	ARfD tyramine children (mg)	Tyramine (mg/kg)	% of contribution in 40 g
Outbreak 1						
Stewed chicken	3.57	<10	-	42.86	58-60	5.41-5.60
Raw chicken		19.9-30.6	22.30-34.29		39.2-118	3.66-11.01
Outbreak 2						
Chicken in sauce	3.57	38.2	42.80	42.86	89	8.31
Outbreak 3						
Chicken in sauce	3.57	48	53.78	42.86	90	8.40
Chicken in sauce		54	60.50		-	-
Frozen chicken thighs		<10	-		75	7.00
Outbreak 4						
Chicken puree	3.57	<10	-	42.86	84	7.84
Chicken in sauce with chopped thighs		23	25.77		79	7.37
Chicken in sauce with thigh fillets		<10	-		102	9.52
Outbreak 5						
Roasted chicken thighs	3.57	<10	-	42.86	15.7	1.47
Frozen chicken thighs		<10	-		114	10.64
Outbreak 6 *						
Raw chicken	3.57	-	-	42.86	71	6.66
Roast chicken		17.9	20.06		104	9.71
Roast chicken		-	-		65.5	6.11
Outbreak 7						
Chicken breast	3.57	33.8	37.87	42.86	166	15.49
Outbreak 8						
Chicken breast	3.57	119	133.33	42.86	265	24.73
Outbreak 9						
Chicken breast	3.57	52	58.26	42.86	181	16.89
Outbreak 10						
Chicken breast	3.57	57	63.87	42.86	157	14.65
Outbreak 11						
Chicken breast	3.57	52	58.26	42.86	136	12.69

Colours: Green, no risk (0-10 %); orange, risk may exist (10-50 %); red, risk exists (> 50 %). * In the case of outbreak 6, the upper margin of the analytical results provided has been used.

For children aged 1-3 years, Table 4 shows the concentrations of biogenic amines with adjusted ARfDs, as well as the % contribution to histamine and tyramine ARfDs when consuming a 40 g portion of the food (FNS, 2018) (EFSA, 2025).

Table 4. Adjusted concentrations of BAs with ARfD in the samples analysed in school canteens

Food	ARfD histamine children (mg)	Histamine (mg/kg)	% of contribution in 40 g	ARfD tyramine children (mg)	Tyramine (mg/kg)	% of contribution in 40 g
Outbreak 1						
Stewed chicken	8.57	<10	-	102.85	58-60	2.26-2.33
Raw chicken		19.9-30.6	9.29-14.28		39.2-118	1.52-4.59
Outbreak 2						
Chicken in sauce	8.57	38.2	17.83	102.85	89	3.46
Outbreak 3						
Chicken in sauce	8.57	48	22.40	102.85	90	3.50
Chicken in sauce		54	25.20		-	-
Frozen chicken thighs		<10	-		75	2.92
Outbreak 4						
Chicken puree	8.57	<10	-	102.85	84	3.27
Chicken in sauce with chopped thighs		23	10.74		79	3.07
Chicken in sauce with thigh fillets		<10	-		102	3.97
Outbreak 5						
Roasted chicken thighs	8.57	<10	-	102.85	15.7	0.61
Frozen chicken thighs		<10	-		114	4.43
Outbreak 6 *						
Raw chicken	8.57	-	-	102.85	71	2.76
Roast chicken		17.9	8.35		104	4.04
Roast chicken		-	-		65.5	2.55
Outbreak 7						
Chicken breast	8.57	33.8	15.78	102.85	166	6.46
Outbreak 8						
Chicken breast	8.57	119	55.54	102.85	265	10.31
Outbreak 9						
Chicken breast	8.57	52	24.27	102.85	181	7.04
Outbreak 10						
Chicken breast	8.57	57	26.60	102.85	157	6.11
Outbreak 11						
Chicken breast	8.57	52	24.27	102.85	136	5.29

Colours: Green, no risk (0-10 %); orange, risk may exist (10-50 %); red, risk exists (>50 %). * The upper margin of the analytical results provided was used in outbreak 6.

Children under the age of 3 have a reduced body weight and their metabolic and enzymatic systems may be immature, so they are particularly sensitive to toxic substances, including biogenic amines. Taking as a reference the experimental data in adults published by various authors, the recommendations of the food safety agencies and the greater sensitivity of children due to the lower body weight, a level of exposure ten times lower (uncertainty factor of 10) could be considered prudent, with respect to the levels considered safe in adults by EFSA. This would imply approximate levels of 2.5 mg/kg histamine and 60 mg/kg tyramine per meal in children under 3 years of age. These values would be, in the vast majority of cases, below the concentrations that caused food poisoning outbreaks in nurseries in some autonomous communities in 2024 (Tables 3 and 4).

However, in order to be able to set safe levels, a number of considerations should be taken into account:

1. Children do not exclusively consume chicken, but the intake of total biogenic amines can be increased through those provided by other foods throughout the day. Therefore, it has been considered that if the percentage of contribution of the biogenic amines assessed (histamine and tyramine) is between 0-10 %, there would be no risk of exceeding the ARfD adjusted for children, between 10-50 % there could be a risk, and above 50 % of contribution due to chicken there would be a risk (Paz et al., 2022).
2. There is a possibility that children are more vulnerable to the effect of biogenic amines mainly due to the immaturity of detoxification systems, including a lower activity of diaminoxidases (DAO).
3. The potentiating effect that the concurrence of the two biogenic amines evaluated or the possible presence of the other biogenic amines could have on toxicity has not been assessed.

Conclusions of the Scientific Committee

Factors that may influence the occurrence of these types of outbreaks

Due to its structure and protein composition, chicken meat is, after fish, the most susceptible to developing biogenic amines. To prevent the formation of biogenic amines, it is essential to use fresh raw materials and have good hygienic conditions, and to use appropriate processing and conservation methods that limit contamination and microbial development, as well as using selected starter cultures that do not produce biogenic amines for the production of fermented products.

The main factors that influence the appearance of outbreaks of food origin associated with the consumption of chicken meat with high concentrations of biogenic amines are, on the one hand, the use of a raw material of low hygienic quality due to poor slaughter and/or processing conditions, which results in a high concentration of microorganisms among which, undoubtedly, producers of biogenic amines will be found. On the other hand, after processing, inadequate or very prolonged transport and/or storage conditions may allow the development of the producing microorganisms.

Acceptable levels of biogenic amines in chicken meat as a whole or if one of them exists as an indicator of a level of risk for the child population under 3 years of age, as well as, where appropriate, for other vulnerable populations

Levels of biogenic amines in fresh chicken meat and products thereof stored and packaged under different conditions vary markedly in the scientific literature. These differences are attributed to the different initial microbiological quality of the meat and the different methods used for the extraction, detection and quantification of biogenic amines.

There is no consensus on the levels of biogenic amines that could be used as a guide in foods, despite their importance with regard to public health. In the European Union, the only biogenic amine that is regulated is histamine (the most toxic biogenic amine), but only in fish and fish products, with maximum limits of 200 and 400 mg/kg, respectively. The American FDA, however, recommends a maximum histamine concentration of 50 mg/kg for foods in general. The EFSA, for its part, has suggested that healthy adults could consume between 25 and 50 mg of histamine and 600 mg of tyramine per meal without presenting adverse effects. Several authors have proposed maximum indices of total biogenic amines or ratios between different biogenic amines (Fraqueza et al., 2012) (Ivanov et al., 2015) (Rodríguez et al., 2015) (Vinci and Antonella, 2002). However, none of these values can be extrapolated directly to children.

There are also a number of uncertainties regarding the toxicity of histamine and tyramine, such as the concurrence of both in the same food, or the potentiating effect that the presence of other biogenic amines may have. Therefore, it is difficult to establish safe maximum levels in this population group.

Finally, although children under 3 years of age are one of the most sensitive sectors of the overall population, even low histamine levels may not be suitable for individuals (children or adults) intolerant to this amine, who require a histamine-free diet.

Aspects related to the production of chicken meat that may have an influence on the level of biogenic amines in chicken meat and whether there is knowledge of changes in chicken rearing systems that may have influenced, such as food, origin, etc.

Although there are differences between different jobs, the concentration of biogenic amines in fresh chicken meat is usually very low, so these compounds do not seem to accumulate in animal tissues. The primary production systems of chicken rearing do not seem to have a decisive influence on the levels of biogenic amines in meat. However, meat production and processing systems can have a great influence on the microbiological contamination of carcasses, which is a critical factor for the formation and accumulation of these amines in meat during its conservation and storage.

Influence of shelf life and storage temperature from the time of slaughter of chickens

The formation of biogenic amines in food is determined by the environmental conditions that allow the development of decarboxylating bacteria and the activity of their enzymes. Processing and storage temperatures and time are critical parameters for the development of these agents and, consequently, for the formation of biogenic amines. To minimize the multiplication of microorganisms and the concomitant production of biogenic amines, perishable products must be kept at tempera-

tures between 0 and 4 °C along the entire processing and transport chain. The work reviewed for the preparation of this report allows us to conclude that, at 4 °C, the production of biogenic amines in chicken meat increases exponentially after 6 days of storage.

Given that the question refers to the time since the slaughter of the chickens, a fact that is not related in some studies, and taking into account that the meat intended for the preparation of food for the child population may have been subjected to a chopping or mincing process that facilitates microbial growth, which has also not usually been considered in the studies, it would be advisable not to use chicken meat with a storage time greater than 5 days after the slaughter of the birds to feed children under 3 years of age, and provided that the meat has been maintained at an adequate temperature since slaughter (0-4 °C).

In view of the above, what measures can minimise the risk in canteens that use this type of meat when the recipients are children under 3 years of age?

To minimise the risk of exposure to biogenic amines in canteens that serve children under 3 years of age, it is essential to apply a set of preventive measures along the entire food chain that include:

1. Selection of high-quality hygienic raw materials.
2. Application of good handling and processing practices.
3. Rigorous control of the cold chain.
4. Careful stock management and menu planning.
5. Training of kitchen and handling staff.

In summary, the effective prevention of the risk from biogenic amines in chicken meat in children's canteens requires a chain of control measures that include the careful selection of raw materials and their proper treatment until their consumption, with special attention to maintaining a suitable refrigeration temperature and storing it for a limited time only.

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