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GENERAL REVIEW

Gut: An underestimated target organ for Aluminum

Le tube digestif : un organe cible sous-estimé pour l'aluminium

C. Vignal^{a,b,*}, P. Desreumaux^{a,b,c}, M. Body-Malapel^{a,b}

^a Université de Lille, LIRIC UMR 995, 59000 Lille, France

^b Inserm, LIRIC UMR 995, 59000 Lille, France

^c CHRU de Lille, LIRIC UMR 995, 59000 Lille, France

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Summary Since World War II, several factors such as an impressive industrial growth, an enhanced environmental bioavailability and intensified food consumption have contributed to a significant amplification of human exposure to aluminum. Aluminum is particularly present in food, beverages, some drugs and airbone dust. In our food, aluminum is superimposed via additives and cooking utensils. Therefore, the tolerable intake of aluminum is exceeded for a significant part of the world population, especially in children who are more vulnerable to toxic effects of pollutants than adults. Faced with this oral aluminum influx, intestinal tract is an essential barrier, especially as 38% of ingested aluminum accumulates at the intestinal mucosa. Although still poorly documented to date, the impact of oral exposure to aluminum in conditions relevant to real human exposure appears to be deleterious for gut homeostasis. Aluminum ingestion affects the regulation of the permeability, the microflora and the immune function of intestine. Nowadays, several arguments are consistent with an involvement of aluminum as an environmental risk factor for inflammatory bowel diseases.

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MOTS CLÉS

Aluminium ;
Exposition orale ;
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intestinale ;

Résumé Depuis la seconde guerre mondiale, plusieurs facteurs tels qu'un essor industriel impressionnant, une augmentation de la bio-accessibilité environnementale et un accroissement de la consommation alimentaire ont contribué à une amplification importante de l'exposition humaine à l'aluminium. L'aluminium est notamment présent dans la nourriture, les boissons, certains médicaments et dans les poussières atmosphériques. Dans notre alimentation, de l'aluminium se rajoute via les additifs et les ustensiles de cuisine. Par conséquent, la dose tolérable d'aluminium est dépassée pour une part significative de la population mondiale,

* Corresponding author at: pôle recherche, faculté de médecine, LIRIC UMR 995, place Verdun, 59045 Lille cedex, France.
E-mail address: cecile.vignal@univ-lille2.fr (C. Vignal).

Colite ;
Maladies
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chroniques de
l'intestin

particulièrement chez les enfants qui sont plus vulnérables aux effets toxiques des polluants que les adultes. Face à cet afflux d'aluminium par voie orale, le tractus intestinal constitue une barrière essentielle, d'autant que 38 % de l'aluminium ingéré s'accumulent au niveau de la muqueuse intestinale. Bien qu'encore peu documenté à ce jour, l'impact de l'exposition orale à l'aluminium en conditions pertinentes par rapport à une exposition humaine réelle semble être délétère pour l'homéostasie de l'intestin. L'ingestion d'aluminium affecte la régulation de la perméabilité, de la microflore et de la fonction immunitaire de l'intestin. De nombreux arguments concordent aujourd'hui vers une implication de l'aluminium en tant que facteur de risque environnemental pour les maladies inflammatoires chroniques de l'intestin.

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Introduction

Aluminum is the third most prevalent element and the most frequent metal in the earth's crust (just after oxygen and silicon). Given to its characteristics (light weight, strength, corrosion resistance), aluminum experienced an annual growth rate of almost 10% over the 1945–1972 because of its increasing intensity of use in building application, basic foils, or aircraft industry. An additional boost in the early 1970s resulted from the development of aluminum beverage cans. Moreover, this growth of aluminum use in industry has been associated with an increase of aluminum environmental bioavailability. Notably, the decline in the use of unprocessed foods and the increased consumption of cakes, pastries, sugar-rich foods characterizing "food westernization" has also occurred. All these combined phenomena have conducted to an enhancement of human oral exposure to aluminum.

The intestinal mucosa constitutes one of the largest surface areas that is exposed to and interacts with the external environment [1]. The small intestine itself is about 300–400 m², which is the size of a tennis court. This large surface area of the gastrointestinal tract (GI tract) plays multiple functionalities, namely absorption of dietary components, immune regulation as well as xenobiotic detoxification, the latter being shared with the liver [2].

Therefore it appears crucial to evaluate precisely the levels and the sources of oral exposure to aluminum, and how the GI tract deals with aluminum which comes into contact with it. Current knowledges on these areas are summarized in this review.

Levels and sources of aluminum oral exposure

Oral exposure of humans to aluminum is mainly from food, beverages, medication and airborne dust. For the general population, most of the daily gastrointestinal intake of aluminum is through the diet. In aluminum workers, it is thought that inhalation will be most important [3].

The levels of aluminum in most food are low but varied within a wide range. In France, the French Food Safety Agency (AFSSA) used a representative market basket of foods commonly prepared for normal consumption which is based on the estimation of the population's dietary intake, to assess the dietary exposure of the population to trace elements, among them aluminum [4]. They found that the French population's mean exposure to aluminum

Table 1 A literature compilation of mean aluminum exposure levels in adults and children.

Compilation des données de la littérature relatives aux niveaux d'exposition à l'aluminium des adultes et des enfants.

Country	Adult mean exposure (µg/kg/day)	Children mean exposure (µg/kg/day)
France	40.3	62.2
Italy	59.6	ND
Spain	175.8	226
United Kingdom	71	155
Canada	124.75	ND
USA	150	ND
Australia	36	44
Japan	42.8	79
China	180.4	471.7

in food is estimated at 40,3 µg/kg bw/day in adults and 62,2 µg/kg bw/day in children (Table 1). The main contributors to aluminum exposure in adults are hot beverages other than coffee (13%), and vegetables excluding potatoes (11%) (Fig. 1). In children, the main contributors are vegetables excluding potatoes (8%), pasta (7%), pastries and cake (6%) and dairy-based desserts (6%) (Fig. 2). In other European countries, the levels of aluminum exposure via food range between 28,6 µg/kg bw/day and 214 µg/kg bw/day with the highest exposure levels in Spain (Canary Islands) for adults and in UK for children [5–8]. Mean exposure level was about 124 µg/kg bw/day in Canada and 180,4 µg/kg bw/day in China (Table 1). The highest exposure levels (471,7 µg/kg bw/day) were observed in Chinese children [9–14]. The health-based guidance value established by the European Food and Safety authority (EFSA) of 1 mg/kg bw/week is thus exceeded by 0,2% of adults and 1,6% of children in France, in a non-negligible part of the population in Canada, China and European countries, considering here food as the sole source of exposure to aluminum [15].

Exposure of infants to aluminum (from birth to 2 years old) is essentially due to consumption of reconstituted or ready-to-use milk- or soy-based formula. Given the vulnerability of infants to toxic chemicals, several studies have evaluated the aluminum content in infant formula. Huge differences were observed between formulas, depending on countries, manufacturer, ingredients..., which globally contained hundred times more aluminum than cow's milk

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