

## Supplement to Hypersensitivity Reactions - The Lalli and Weber Effects

When using contrast media in medical imaging the user should be aware about two linked effects that may influence the frequency of acute hypersensitivity reactions, the Lalli and Weber effects.

### *Lalli Effect*

In the heydays of high osmolar ionic contrast media use in the 1970s it was demonstrated that fear and anxiety play an important role in the occurrence of hypersensitivity reactions to iodine-based contrast media (ICM), now termed the Lalli effect (Lalli, 1974; Thomsen, 2012). Anxiety causes the limbic system to interact with the hypothalamus. As contrast media pass the blood-brain barrier, it can interact with the hypothalamus and reticular formation of the medulla. In the hypothalamus the vasomotor system and respiratory system can become activated, leading to shock or respiratory arrest. Reticular formation activation can lead to nausea and emesis, as well as vagal reactions with bradycardia, hypotension, and bronchospasm. Finally, in the ventral and lateral funiculi of the spinal cord and in the stellate ganglion the sympathetic autonomous nervous system can become activated, which may result in pulmonary oedema, skin urticaria, or even ventricular fibrillation or cardiac arrest (Lalli, 1980 and 1981). It was shown that diazepam may be beneficial in apprehensive patients scheduled for imaging with ICM (Lalli, 1981).

### *Weber Effect*

The Weber effect is a well-known reporting bias from pharmacovigilance studies. The reporting of adverse effects after regulatory approval of a drug to the market peaks at the end of the second year after approval, and declines steadily thereafter (Weber, 1984). In the field of contrast media this effect has been demonstrated for gadopentetate (Aran, 2014) and for gadobenate (Fakhran, 2015). It was also demonstrated for nonsteroidal anti-inflammatory drugs (Hartnell, 2004), but could not be demonstrated for other drugs in the same Food & Drug Administration's Adverse Events Registration System (FAERS) (Hoffman, 2014). In daily medical imaging practice, it is important to realize that when one specific contrast medium is substituted for another, a significant transient increase in the frequency of reported hypersensitivity reactions may be seen (Davenport, 2013; Forbes-Amrhein, 2018).

## Literature

Aran S, Shaqdan K, Abujudeh H. The Weber effect; A multi-year experience with gadopentetate dimeglumine administration. Radiological Society of North America 2014 Scientific Assembly and Annual Meeting, Chicago IL. Available at: [\[URL\]](#). Accessed May 20, 2022.

Davenport MS, Dillman JR, Cohan RH, Hussain HK, Khalatbari S, McHugh JB, Ellis JH. Effect of abrupt substitution of gadobenate dimeglumine for gadopentetate dimeglumine on rate of allergic-like reactions. *Radiology*. 2013; 266(3): 773-782.

Fakhran S, Alhilali L, Kale H, Kanal E. Assessment of rates of acute adverse reactions to gadobenate dimeglumine: review of more than 130,000 administrations in 7.5 years. *AJR Am J Roentgenol*. 2015; 204(4): 703-706.

Forbes-Amrhein MM, Dillman JR, Trout AT, Koch BL, Dickerson JM, Giordano RM, Towbin AJ. Frequency and severity of acute allergic-like reactions to intravenously administered gadolinium-based contrast media in children.

- Invest Radiol. 2018; 53(5): 313-318.
- Hartnell NR, Wilson JP. Replication of the Weber effect using post-marketing adverse event reports voluntarily submitted to the United States Food and Drug Administration. *Pharmacotherapy* 2004; 24(6): 743–749.
- Hoffman KB, Dimbil M, Erdman CB, Tatonetti NP, Overstreet BM. The Weber effect and the United States Food and Drug Administration's Adverse Event Reporting System (FAERS): analysis of sixty-two drugs approved from 2006 to 2010. *Drug Saf.* 2014; 37(4): 283-294.
- Lalli AF. Urographic contrast media reactions and anxiety. *Radiology.* 1974; 112(2): 267-271. Lalli AF. Contrast media reactions: data analysis and hypothesis. *Radiology.* 1980; 134(1): 1-12.
- Lalli AF, Greenstreet R. Reactions to contrast media: testing the CNS hypothesis. *Radiology.* 1981; 138(1): 47-49.
- Thomsen HS, Webb JAW. The Lalli and Weber effects and the incidence of acute non-renal adverse reactions to contrast media. *Acta Radiol.* 2012; 53(9): 953-954.
- Weber JCP. Epidemiology of adverse reactions to nonsteroidal anti-inflammatory drugs. In: Rainsford KD, Velo GD, editors. *Side-effects of Anti-inflammatory Drugs, Advances in Inflammation Research.* New York: Raven Press; 1984: 1–7.