

Allergies & Essure

Real-world Challenges

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Medical Device Problems



DISCLOSURES



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**Not a litigant
or witness**



**No financial
conflicts of interest**

How did we get here?

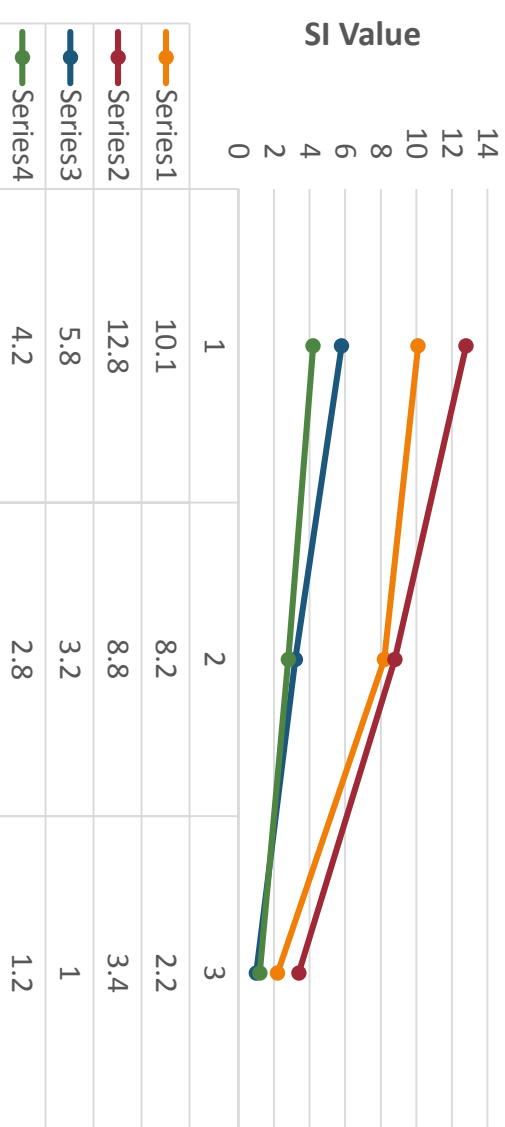
“...there was no criteria per se in the studies to identify or to say this is an allergic reaction. So we also do not have that.”^[1]



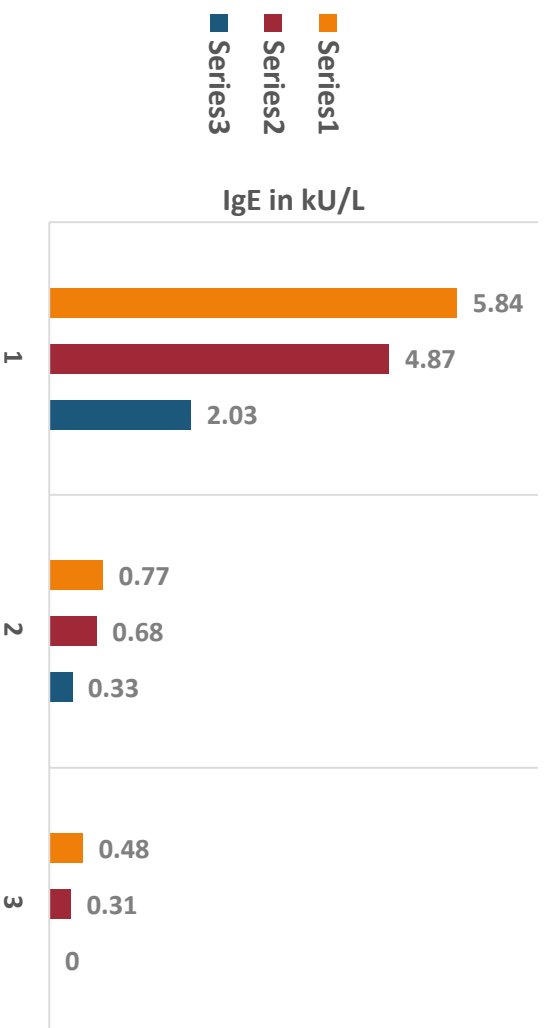
MY PERSONAL DATA

- **SOD2 rs4880 (AG):** variant (G) Multiple Chemical Sensitivity^[2,3]
- **MTHFR A1298C rs1801131 (GT):** variant (G) hypersensitivity to Hg PON1 rs662 (TT): variant (T)^[4]
- **MTHFR C677T rs1801133 (GA):** variant (A) migraine with aura^[5]
- **CYP2R1 rs10741657(AG):** allele (G) Vitamin D insufficiency
- **CYP2R1 rs12794714(AG)^[6]**

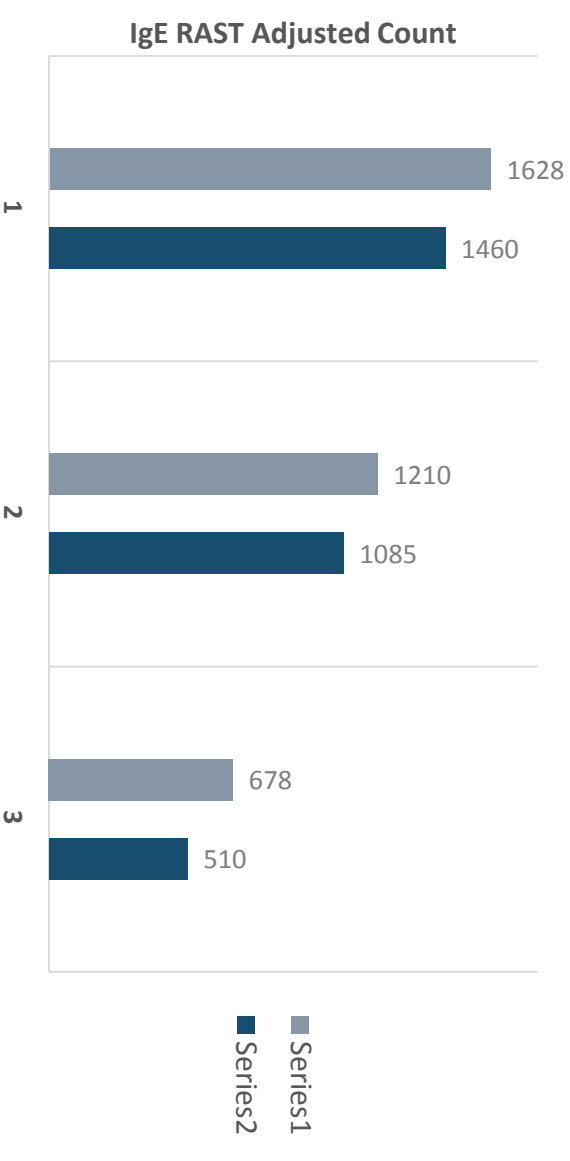
NEW-ONSET METAL ALLERGIES



NEW-ONSET FOOD ALLERGIES



NEW-ONSET DRUG ALLERGIES



Essure Adverse Events*

- **14,471** auto-immune^[7]
- 7,293 migrations/perforations
- 7,401 migraines^[8,9]
- **6,581** allergy
- **5,774** skin symptoms^[10,11]
- 1,966 endometriosis^[12]
- 845 vitamin D deficiency^[13]
- 223 hormonal imbalance^[14]
- **120** multiple allergies
- **40** anaphylaxis
- 7 tattoo site dermatitis^[15]



*data courtesy of Device Events™

Physician Hurdles

- Poor labeling
- Poor communication
- Disparate health systems
- Poor access to AE data
- Constellation of symptoms
- Limitations of tests
- Costs to patient/insurance

“...it ends up being an exclusion at the end of the day, that you just rule out what it is and what *might* be the cause...”^[1]



We can do better!

Genetic Tests

- FLG^[16]
- TLR5
- TLR4^[17]
- SOD
- HLA^[18]
- MTHFR



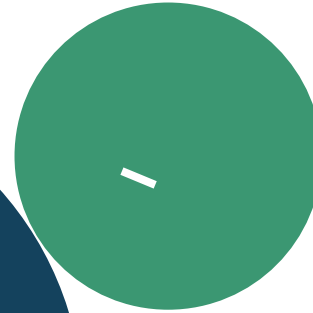
1.Tools

2.Expertise

3.Will

Allergy Tests

- LTT or LPT
- IgE Tests
- Patch Tests



Blood Tests

- Vitamin D
- Estrogen/Hormone
- Cytokine Panels ^[19]



Communication

- Medical history
- Plain language
- Better records



REFERENCES

1. USA DHHS FDA CDHR. (2015, Sep. 24). *Meeting of The Obstetrics & Gynecology Devices Panel*, 203-205.
2. Cui, X., Lu, X., Hiura, M., Oda, M., Miyazaki, W., & Katoh, T. (2013). Evaluation of genetic polymorphisms in patients with multiple chemical sensitivity. *PLoS one*, *8*(8), e73708. doi:10.1371/journal.pone.0073708
3. Krause, M. E., Glass, A. M., Jackson, T. A., & Laurence, J. S. (2010). Novel tripeptide model of nickel superoxide dismutase. *Inorganic chemistry*, *49*(2), 362–364. doi:10.1021/ic901828m
4. Austin, D. W., Spolding, B., Gondalia, S., Shandley, K., Palombo, E. A., Knowles, S., & Walder, K. (2014). Genetic variation associated with hypersensitivity to mercury. *Toxicology international*, *21*(3), 236–241. doi:10.4103/0971-6580.155327
5. Liu, A., Menon, S., Colson, N. J., Quinlan, S., Cox, H., Peterson, M., ... Griffiths, L. R. (2010). Analysis of the MTHFR C677T variant with migraine phenotypes. *BMC research notes*, *3*, 213. doi:10.1186/1756-0500-3-213
6. Wang, T. J., Zhang, F., Richards, J. B., Kestenbaum, B., van Meurs, J. B., Berry, D., ... Spector, T. D. (2010). Common genetic determinants of vitamin D insufficiency: a genome-wide association study. *Lancet (London, England)*, *376*(9736), 180–188. doi:10.1016/S0140-6736(10)60588-0
7. Bjørklund G., Dadar M., Aaseth J. (2018). Delayed-type hypersensitivity to metals in connective tissue diseases and fibromyalgia. *Environmental Research*, *161*, 573-579. doi: 10.1016/j.envres.2017.12.004.
8. Wertman, B., Azarbal, B., Riedl, M., & Tobis, J. (2006). Adverse Events Associated With Nickel Allergy in Patients Undergoing Percutaneous Atrial Septal Defect or Patent Foramen Ovale Closure. *Journal of the American College of Cardiology*, *47*(6), 1226-1227.
9. Kato, Y., Furuya, D., Ishido, H., Kobayashi, T., & Tanahashi, N. (2012). New-onset migraine with aura after transcatheter closure of atrial septal defect. *The Journal of Headache and Pain*, *13*(6), 493-495.
10. Bogdali M. A., Antoszczyk G., Dyga W., Obtulowicz A., Bialecka A., Kasprowicz A. et al. (2016). Nickel allergy and relationship with Staphylococcus aureus in atopic dermatitis. *Journal of Trace Elements in Medicine and Biology*, *33*, 1-7. doi: 10.1016/j.jtemb.2015.06.009
11. Remy L., et al. (2012). The Staphylococcus aureus Opp1 ABC transporter imports nickel and cobalt in zinc-depleted conditions and contributes to virulence. *Molecular Microbiology*, *87*(4), 730-743.
12. Yuk, J., Kim, Y., Yi, K., Tak, K., Hur, J., & Shin, J. (2015). High rate of nickel allergy in women with endometriosis: A 3-year population-based study. *Journal of Obstetrics and Gynaecology Research*, *41*(8), 1255-1259.
13. Hoxha, M., Zoto, M., Deda, L., & Vyshka, G. (2014). Vitamin D and Its Role as a Protective Factor in Allergy. *International Scholarly Research Notices*, *2014*(2014).
14. Fan Z., Che H., Yang S., Chen C. (2019). Estrogen and estrogen receptor signaling promotes allergic immune responses: Effects on immune cells, cytokines, and inflammatory factors involved in allergy. *Allergologia et Immunopathologie*, *47*, 506-12. doi: 10.1016/j.aller.2019.03.001
15. Cobb, H. K., Shinohara, M. M., Huss, J. T., Welch, M. P., & Gardner, J. M. (2017). Systemic contact dermatitis to a surgical implant presenting as red decorative tattoo reaction. *JAAD case reports*, *3*(4), 348–350. doi:10.1016/j.jdcr.2017.05.003.
16. Ross-Hansen K., Ostergaard O., Tanassi J.T., Thyssen J.P., Johansen J.D., Menne T. et al. (2014). Filaggrin Is a Predominant Member of the Denaturation-Resistant Nickel-Binding Proteome of Human Epidermis. *Journal of Investigative Dermatology*, *134*(4), 1164-1166. doi:10.1038/jid.2013.445 Peripheral Blood Mononuclear Cell Cultures from Nickel-Allergic Individuals. *International Archives of Allergy and Immunology*, *132*, 373-379. doi: 10.1159/000074905.
17. Schmidt, M. & Goebeler, M. (2011). *Journal of Molecular Medicine* *89*, 961. doi: 10.1007/s00109-011-0780-0.
18. Wang, Y., & Dai, S. (2013). Structural basis of metal hypersensitivity. *Immunologic research*, *55*(1-3), 83–90. doi:10.1007/s12026-012-8351-1
19. Cederbrant K, Anderson C, Andersson T, Marcusson-Ståhl M, Hultman P (2003). Cytokine Production, Lymphocyte Proliferation and T-Cell Receptor Vβ Expression in Primary Peripheral Blood Mononuclear Cell Cultures from Nickel-Allergic Individuals. *International Archives of Allergy and Immunology*, *132*, 373-379. doi: 10.1159/000074905.