Increased serum serotonin after triannual pollen events as a cause of cardiac arrest spikes in the U.S.

## Tariq Khan Omaha, Nebraska, USA

The United States ecosystem has three major pollenating species (juniper, grass, and ragweed) creating a triannual cycle. That cycle involves increases in environmental pollen leading to the physiological increase in serum histamine and then the eventual subsequent decrease in pollen and histamine leading to a biochemical increase in serum serotonin. This increase in serotonin matches year-over-year patterns in mass shootings, speculative stock buying, and even cardiac arrests (heart attacks) in the United States. Understanding the nature of the cause of heart attacks where weaker or older hearts are strained directly or indirectly from these serotonin "spikes," the medical community can work to treat those scenarios (adding or reducing meds or activity) potentially saving thousands of lives.

Because of mast cell involvement in these clinical syndromes... there has been great interest in the pharmacological modulation of histamine release from mast cells. Serotonin is also stored in mast cell granules. Because histamine and serotonin may have divergent functions in delayed hypersensitivity, we hypothesized that these amines could undergo differential release. -- Nature

Mast cells also emit serotonin, a mood-modifying molecule. -- Science

Mast cells are a source of serotonin... We conclude that mast cells contribute to behavioral and physiological functions of the hippocampus... It is known that mast cells can synthesize and store serotonin... The hippocampus is important in the regulation of anxiety and depressive behaviors ...

-- The European Journal of Neuroscience

"We human beings are part of nature and therefore we are more likely to find out about our 'inner' nature, to understand ourselves, by looking outside ourselves, at our role and place as animals. In John Gray's words, 'A zoo is a better window from which to look out of the human world than a monastery.' This is not paradoxical, and without some such realignment of approach, the modern incoherence will continue."

-- Peter Watson -- Ideas a history of thought and invention, from fire to Freud

**Serotonin**: ...serotonergic neurons ... play an important part in a variety of psychiatric conditions from anxiety disorders to schizophrenia as well as behavioral impulse-related disorders (violence, substance abuse, obsessive control, etc....)

The large scale analysis of medical and societal challenges in the United States and the world can or could be approached by using more of holistic or systems approach using techniques from physics and economics. Another point of consideration is that of omission bias. Of particular interest in this paper is the inverse relationship of histamine and serotonin within the human body (Hough, 1999, and Munari et. al., 2015, and Ryo et. al., 2006). Note also that male humans have 52% more serotonin than females (Nishizawa et. al., 1997). So much obvious attention is paid to the personal health challenges that each tree, grass, and weed pollen season brings with breathing, asthma, sinus ailments, poor sleep, skin reactions, etc. But little attention is paid to the period of time (and biochemical consequences) when pollen and thus serum histamine drop after a given pollen "season" or when pollen levels drop suddenly. It is this omission bias that has led to the scientific community missing some stunning observations or correlations involving major behaviors of individuals and large populations of humans in the United States.

The United States ecosystem has three major pollenating species (juniper tree, grass, and ragweed weed) creating a triannual cycle. That cycle involves increases in environmental pollen leading to a physiological increase in serum histamine and then the subsequent decrease in pollen and histamine leading to a biochemical increase in serum serotonin. This increase in serotonin matches year-over-year patterns in mass shootings (**Fig. 1-2**), speculative stock buying (**Fig. 3-4**), and even cardiac arrests (heart attacks) (**Fig. 5-7**). An examination of monthly heart attacks, averaged out in a given US location or the entire country, should thus show corresponding spikes at the end of juniper tree pollen season (mid to late March), summer grass pollen (mid to end July) and fall ragweed pollen (end September to November) (**Fig. 5-7**). This is obviously separate from the grander U-shaped annual trend of heart attacks corresponding to the impact of winter and cold temperature related physical stress e.g., snow shoveling, daylight savings time adjustments, and holiday binging of food and alcohol, which are known causes of wintertime heart attacks.

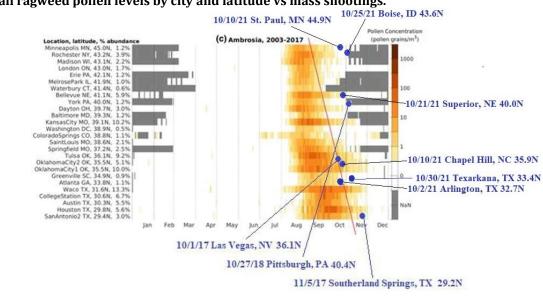
Indirectly, increased serotonin can cause or induce other medical conditions like asthma. In 2020, Dr. David Artis noted in his research on allergic inflammation that "prior research also has linked elevated serotonin levels to asthma." In 2005, research by G Krommydas et al. showed that "serotonin may actually cause bronchoconstriction, thus cancelling the beneficial effects of these drugs to airways. Serotonin induces bronchoconstriction via peripheral and central pathways resulting in increasing colinergic activity and histamine release." Also, ScienceDaily reported in 2021 that Uppsala University research by Erika Mendez-Enriquez et al. showed that the "release of serotonin from mast cells contribute to airway hyperresposivness in asthma."

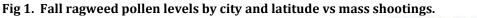
Thus, understanding the nature of the heart attacks where weaker or older hearts are strained directly or indirectly from these triannual serotonin "spikes," the medical community can work to treat those scenarios (adding or reducing meds or activity) potentially saving thousands of lives. In essence, clinicians could treat patients as if they were at risk of minor "serotonin syndrome" symptoms during those three times of years. Medications could be used for those one or two weeks to lower serotonin to reduce heart attack risks like cromolyn salt (via mast cell interruption). Other examples from the Mayo Clinic website include:

- Muscle relaxants or benzodiazepines, such as diazepam (Valium, Diastat) or lorazepam (Ativan) or Lunesta.
- Serotonin-production blocking agents like cyproheptadine.
- Drugs that control heart rate and blood pressure like esmolol (Brevibloc) or nitroprusside (Nitropress).

Another interesting observation is the common trend of elderly retirees moving to southern Florida. Not only do they gain the benefit of higher amounts of sunlight, shown to lower blood pressure and thus lifespan, they also have moved into a very low ragweed and overall low pollen environment and thus have a reduced chance of having post-pollen-cycle high serotonin induced cardiac arrests. A wise choice of retirement location indeed by the snowbird population.

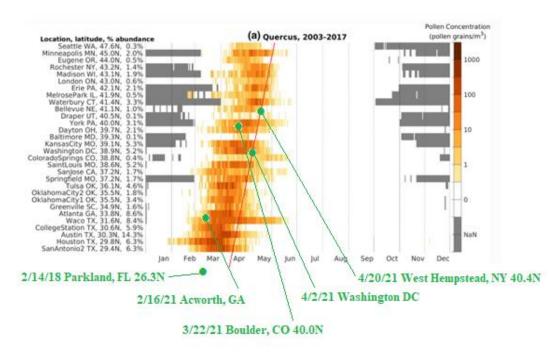
## Figures



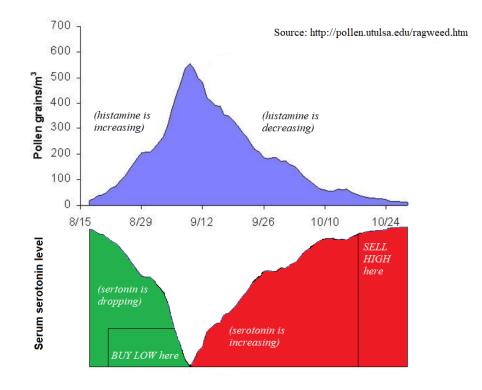


Source: https://link.springer.com/article/10.1007/s10453-019-09601-2

## Fig. 2. Spring tree pollen levels by city and latitude vs mass shootings.



Source: https://link.springer.com/article/10.1007/s10453-019-09601-2



# Fig 3. "BUY and SELL" strategy timeline vs fall ragweed allergen and serotonin levels.

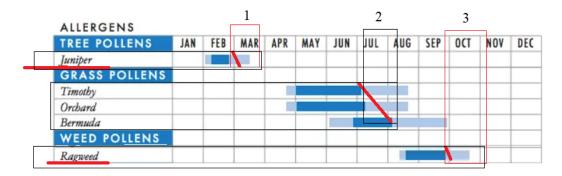
## Fig 4. Robinhood SPDR S&P 500 ETF indexed fund (fall 2021) showing "J" shaped movement.

8/20/2021	\$100.00 purchased to monitor.
9/16/2021	\$100.87 baseline
10/4/2021	\$96.69 (low buy)
11/5/2021	\$106.10 (high sell) 32 days later (25 trading days) = 9.7% growth rate.



Source: Robinhood android smartphone app display of SYDR SAP 500 ETF fund retrieved 11/5/2021.

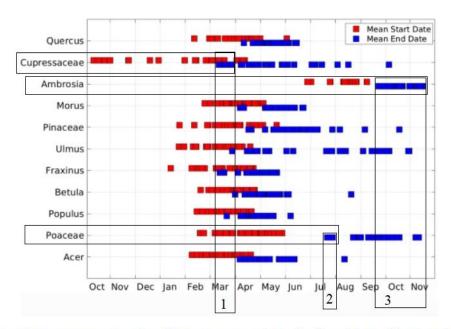
## Fig. 5. Primary US tree, grass, and weed pollen months with declines matching serotonin spikes.



This chart shows the pollen peaks for various species in the mid-Atlantic region of the US. Tree pollen peaks in the spring, grass pollen peaks in the summer, and weed pollen peaks in the fall. | Johns Hopkins University, Division of Allergy and Clinical Immunology

Source: https://www.vox.com/2020/5/7/21250550/allergy-season-2020-pollen-climate-change-coronavirus-pandemic

## Fig. 6. Primary US tree, grass, and weed pollen months with declines matching serotonin spikes.



Range of long-term mean main pollen season start dates (red), end dates (blue), and duration (green) for important pollen taxa; each square represents the long-term mean of a NAB station

Source: https://link.springer.com/article/10.1007/s10453-019-09601-2/figures/6

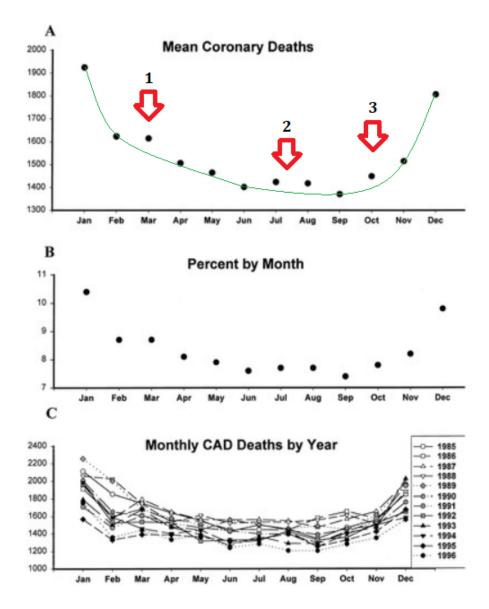


Fig. 7. Example of US cardiac arrests by months vs "serotonin spikes" after triannual pollen events.

Source: https://www.ahajournals.org/doi/full/10.1161/01.CIR.100.15.1630

#### References

- Allergy cells in the rodent brain may keep baseline anxiety under control. 2008. Immune to Anxiety. Science. Retrieved from <u>https://www.science.org/content/article/immune-anxiety</u> November 11, 2021.
- Fatih Hilmi Çetin, Yasemin Taş Torun and Esra Güney (July 26th, 2017). The Role of Serotonin in Aggression and Impulsiveness, Serotonin - A Chemical Messenger Between All Types of Living Cells, Kaneez Fatima Shad, IntechOpen, DOI: 10.5772/intechopen.68918. Retrieved from: <u>https://www.intechopen.com/books/serotonin-a-chemical-messenger-between-all-types-of-livingcells/the-role-of-serotonin-in-aggression-and-impulsiveness</u>
- Ferri, Fred F. (2016). Ferri's Clinical Advisor 2017: 5 Books in 1. Elsevier Health Sciences. pp. 1154–1155. ISBN 9780323448383.
- Hough LB. Histamine Actions in the Central Nervous System. In: Siegel GJ, Agranoff BW, Albers RW, et al., editors. Basic Neurochemistry: Molecular, Cellular and Medical Aspects. 6th edition. Philadelphia: Lippincott-Raven; 1999. Retrieved from: https://www.ncbi.nlm.nih.gov/books/NBK28245/
- Krommydas, G et al. 2005. Antidepressants And Asthma Treatment. The Internet Journal of Pulmonary Medicine. 2005 Volume 6 Number 1. Retrieved from: https://ispub.com/IJPM/6/1/10432 November 11, 2021.
- Le, Jandy, Xiong, Michael, and Joshi Jwalin. 2019. *The Scientific Origin of Creativity*. Neurotech@Berkeley. Retrieved from: <u>https://medium.com/neurotech-berkeley/the-scientific-origin-of-creativity-</u>587799f0fbe2 October 31, 2021.
- Leonardo Munari, PhD, Gustavo Provensi, PhD, Maria Beatrice Passani, PhD, Nicoletta Galeotti, PhD, Tommaso Cassano, PhD, Fernando Benetti, PhD, Renato Corradetti, MD, Patrizio Blandina, MD, Brain Histamine Is Crucial for Selective Serotonin Reuptake Inhibitors' Behavioral and Neurochemical Effects, International Journal of Neuropsychopharmacology, Volume 18, Issue 10, September 2015, pyv045, <u>https://doi.org/10.1093/ijnp/pyv045</u>. Retrieved from: https://academic.oup.com/ijnp/article/18/10/pyv045/623738
- Mayo Foundation for Medical Education and Research. (2019, December 10). *Serotonin syndrome*. Mayo Clinic. Retrieved November 13, 2021, from <u>https://www.mayoclinic.org/diseases-conditions/serotonin-syndrome/diagnosis-treatment/drc-20354764</u>.
- Nautiyal, K. M., Dailey, C. A., Jahn, J. L., Rodriquez, E., Son, N. H., Sweedler, J. V., & Silver, R. (2012). Serotonin of mast cell origin contributes to hippocampal function. The European journal of neuroscience, 36(3), 2347–2359. https://doi.org/10.1111/j.1460-9568.2012.08138.x Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3721752/ November 12, 2021.
- Nishizawa, S., Benkelfat, C., Young, S. N., Leyton, M., Mzengeza, S., de Montigny, C., Blier, P., & Diksic, M. (1997). Differences between males and females in rates of serotonin synthesis in human brain. Proceedings of the National Academy of Sciences of the United States of America, 94(10), 5308–5313.
  <u>https://doi.org/10.1073/pnas.94.10.5308</u> Retrived from: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC24674/</u>
- Ryo Yoshimoto, Yasuhisa Miyamoto, Ken Shimamura, Akane Ishihara, Kazuhiko Takahashi, Hidehito Kotani, Airu S. Chen, Howard Y. Chen, Douglas J. MacNeil, Akio Kanatani, Shigeru Tokita. Therapeutic potential of histamine H3 receptor agonist for the treatment of obesity and diabetes mellitus. Proceedings of the National Academy of Sciences Sep 2006, 103 (37) 13866-13871; DOI: 10.1073/pnas.0506104103. Retrieved from: https://www.pnas.org/content/103/37/13866

- Theoharides, T., Bondy, P., Tsakalos, N. et al. Differential release of serotonin and histamine from mast cells. Nature 297, 229–231 (1982). https://doi.org/10.1038/297229a0 retrieved from: https://www.nature.com/articles/297229a0 November 11, 2021.
- Mendez-Enriquez, Erika et al. Uppsala University. 2021, March 12. Release of serotonin from mast cells contribute to airway hyperresposivness in asthma. ScienceDaily. Retrieved November 13, 2021, from www.sciencedaily.com/releases/2021/03/210312121314.htm
- Artis, David. 2020. Scientists Identify New Pathways to Inflammation in Allergy-Linked Immune Cells. Https://News.Weill.Cornell.Edu. Retrieved November 13, 2021, from <u>https://news.weill.cornell.edu/news/2020/04/scientists-identify-new-pathways-to-inflammation-in-allergy-linked-immune-cells</u>