musc Children's Health
Medical University of South Carolina

MUSC Otolaryngology Literature Course 2024

PEDIATRIC OTOLARYNGOLOGY

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Pediatric Otolaryngology

Disclosures

- None

This year

- …

Environmental Risk Factors for Pediatric Epistaxis vary by Climate Zone

Eric X. Wei, MD; Allen Green, BS; Michael T. Chang, MD; Peter H. Hwang, MD; Douglas R. Sidell, MD; Z. Jason Qian, MD

https://www.michiganmedicine.org/health-lab/what-causes-nosebleeds-children

- March 2024
- Laryngoscope
- Stanford

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Eric X. Wei, MD; Allen Green, BS; Michael T. Chang, MD; Peter H. Hwang, MD; Douglas R. Sidell, MD; Z. Jason Qian, MD

- Background:
  - Nosebleeds are very common
  - Affects 30% of children 0-5 years of age and over half of kids over age 5.
  - Majority spontaneous and self resolving
  - Most previous studies say cold/dry weather is bad - but more recently this is called into question.

Environmental Risk Factors for Pediatric Epistaxis vary by Climate Zone

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- Objective: "… to investigate correlations between season, temperature and humidity on frequency of pediatric epistaxis across climate zones"
- Why? Authors say – "Prior studies have provided variable results..." and "These studies were conducted in varying climate zones." Also, mostly single institution investigations that didn't work across climate zones.
  - "With increasing awareness of climate change and its impact on severe weather fluctuations and human health, a growing body of literature has emerged exploring relationships between meteorological factors such as temperature, humidity and seasonality with incidence of common medical conditions such as epistaxis."

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- Study Design (**DEFINE EXPERIMENTAL GROUP**)
  - Insurance claims data from - IBM Watson Health MarketScan Research Database (publicly available for a fee per year of data)
    - This source encompassed the longitudinal health care claims of approximately 180 million unique enrollees of qualifying employer sponsored health insurance plans. This database is publicly available for researchers for a fee per year of data. (all privately insured)
  - 2007 – 2010 (the only years where granular county level data were available). ??
  - Under 18
  - ICD 9 and ICD 10 (784.7 and R04.0) to capture experimental cohort.

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- Study Design: (**DEFINE EXPERIMENTAL GROUP**)
  - Children who went on to receive cauterization were identified by CPT codes:
    - 30901 - Control nasal hemorrhage, anterior, simple (limited cautery and/or packing) any method
    - 30903 - Control nasal hemorrhage, anterior, complex (extensive cautery and/or packing) any method
    - 30905 - Control nasal hemorrhage, posterior, with posterior nasal packs and/or cautery, any method; initial
    - 30906 - Control nasal hemorrhage, posterior, with posterior nasal packs and/or cautery, any method; subsequent
    - 31231 - Nasal endoscopy, diagnostic, unilateral or bilateral (separate procedure)
    - 31238 - Nasal/sinus endoscopy, surgical; with control of nasal hemorrhage
  - "Notably, we did not include CPT codes for sphenopalatine, internal maxillary, and ethmoid artery ligation because (1) specific CPT codes for these procedures did not exist for the majority of the study period, and (2) these procedures would represent extreme cases in the pediatric population, which was not the focus of this epidemiologic study."

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- Study Design: (**DEFINE CONTROL GROUP**)
  - Control Group
    - A control cohort of children who received well-child visits (with no other diagnoses) were identified by ICD-9 V20.2 and ICD-10 Z00.129.
      - V20.2 – Routine infant or child health check
      - Z00.129 – Encounter for routine child health examination without abnormal findings.
  - Pruned to a 10% random sample for the final analyses. Does not say how this was done

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- Study Design: (**DEFINE SEASON OF VISIT**)
  - Season
    - Meteorologic season of the visit was identified by service date, where December–February was winter, March–May was spring, June–August was summer, and September–November was fall. Seasons represent a combination of temperature and humidity with winter having cooler temperature and lower relative humidity than the summer.
    - **You're WELCOME!**

https://x.com/daknowledgebomb

Environmental Risk Factors for Pediatric Epistaxis vary by Climate Zone

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- Study Design: (**DEFINE WHERE**)
  - County of residence as identified by Federal Information Processing Standard (FIPS) code were obtained from the database.
    - What is FIPS?!
    - Federal govt has codes for each country and county for all databases.

38	NORTH DAKOTA
39	OHIO
40	OKLAHOMA
41	OREGON
42	PENNSYLVANIA
44	RHODE ISLAND
45	SOUTH CAROLINA
46	SOUTH DAKOTA
47	TENNESSEE
48	TEXAS
49	UTAH
50	VERMONT
51	VIRGINIA
53	WASHINGTON
54	WEST VIRGINIA
55	WISCONSIN
56	WYOMING

county-level FIPS code	place name
01000	Alabama
01001	Autauga County
01003	Baldwin County
01005	Barbour County
01007	Bibb County
01009	Blount County
01011	Bullock County
01013	Butler County
01015	Calhoun County
01017	Chambers County
01019	Cherokee County
01021	Chilton County
01023	Choctaw County
01025	Clarke County
01027	Clay County
01029	Cleburne County
01031	Coffee County
01033	Colbert County
01035	Conecuh County

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- Study Design: (**DEFINE WHERE - CLIMATE / HUMIDITY**)
  - Climates and humidity:
    - Climates were assigned - International Energy Conservation Code (IECC) climate zone classification.
    - IECC classifies climate in the United States by temperature zone from 1 (extremely hot) to 8 (subarctic/arctic) and humidity (moist, dry, or marine). Notably, temperature zones from 1–6 may be assigned moist or dry humidity; temperature zones 3–5 may assigned moist, dry, or marine humidity; and temperature zones 7–8 are not assigned humidity.

Doesn't make any sense without a map!

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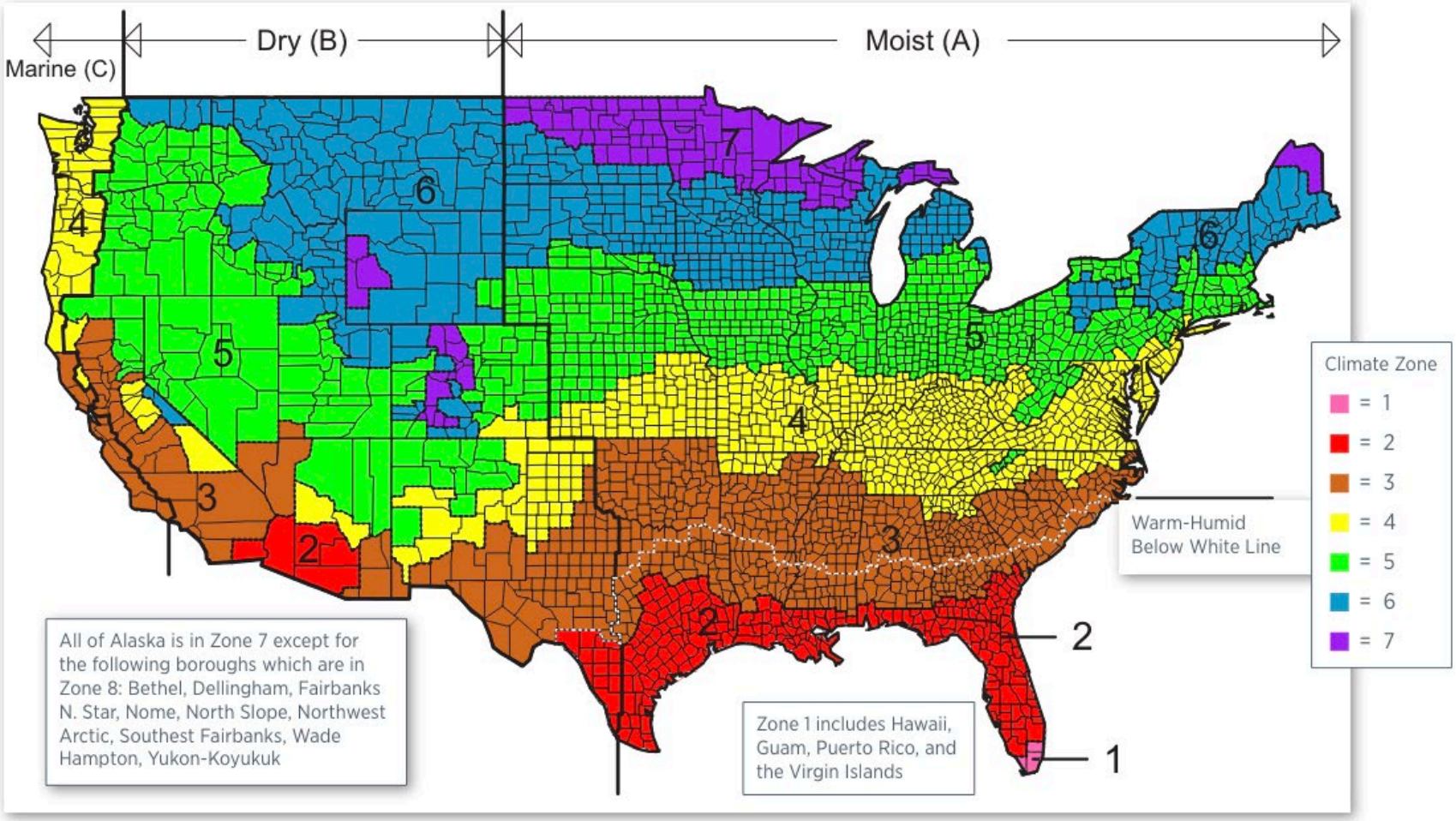

https://www.energy.gov/sites/prod/files/2015/10/f27/ba_climate_region_guide_7.3.pdf

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- Study Design:
  - Stats: Statistical analyses were performed with Stata 16 (StataCorp, College Station, TX). For statistical analyses, only the first incidence of epistaxis was used for each subject.

Environmental Risk Factors for Pediatric Epistaxis vary by Climate Zone

Eric X. Wei, MD; Allen Green, BS; Michael T. Chang, MD; Peter H. Hwang, MD; Douglas R. Sidell, MD; Z. Jason Qian, MD

- Results: (A FEW BROAD STROKES HERE)
  - 184,846 kids in epistaxis group vs 1,869,756 in control group
  - 299,694 visits for epistaxis
  - Control group 51% male, epistaxis group 60% male
  - Median age epistaxis group 9 years
  - About 11% of kids in epistaxis group got cautery (93% of these in office, 4.3% ER and 2.3% OR)

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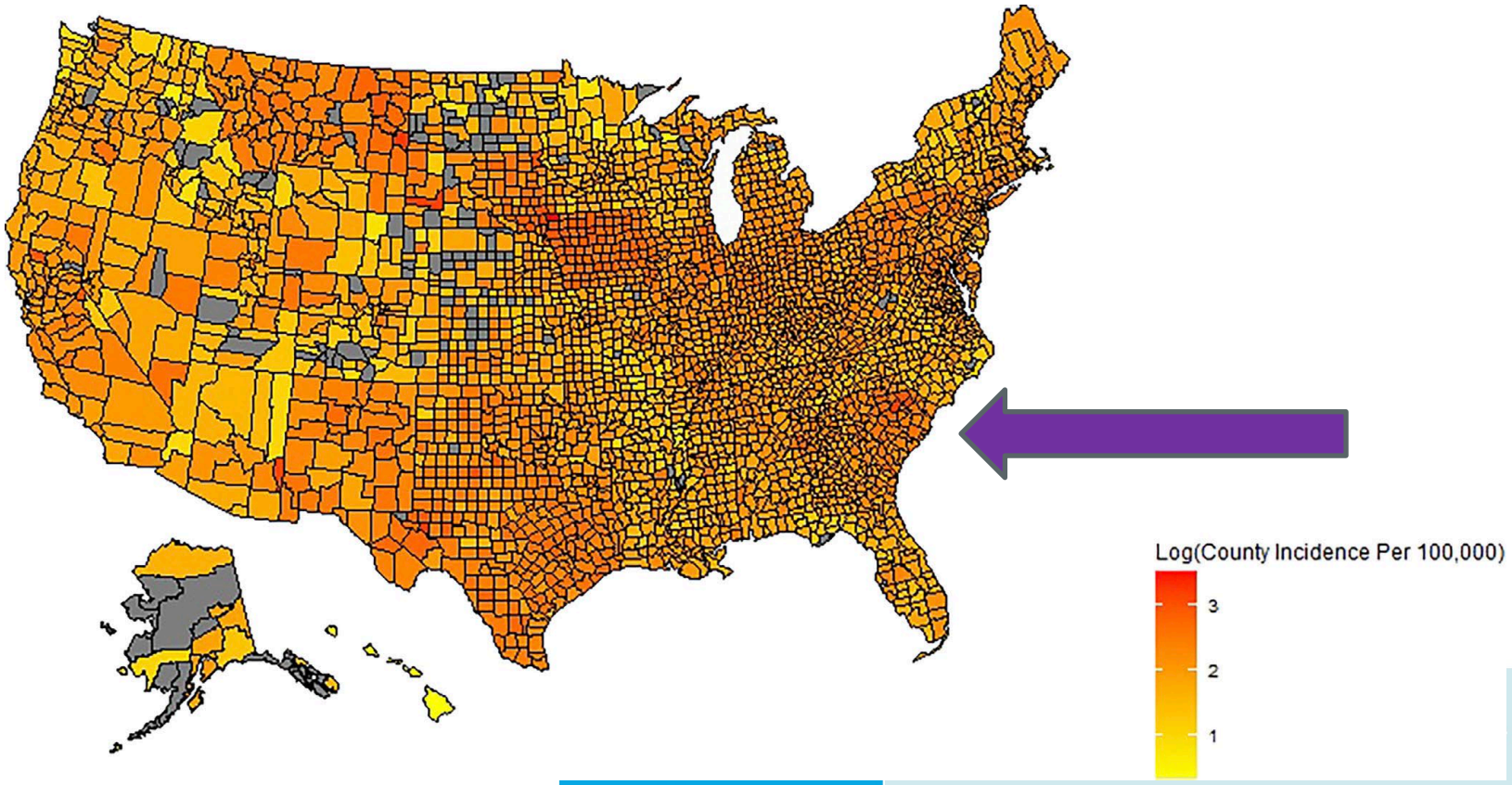
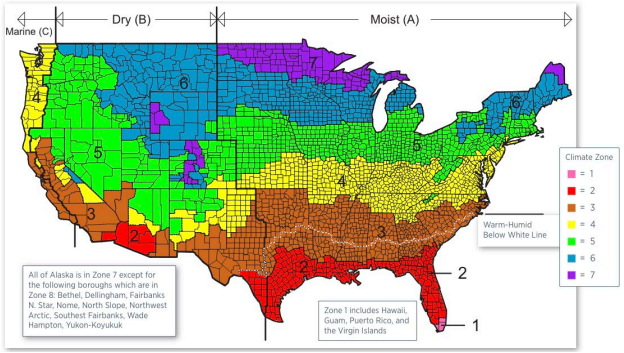
- Results:
  - The majority of US counties (3115/3241 FIPS codes [96.1%]) were represented in this sample.





- Just shows basic breakdown of the groups here

TABLE I.
Characteristics of Study Population by Temperature and Humidity Zones.

		Epistaxis (n = 184,846)***	
	Control (n = 1,869,756)	No Cautery (n = 164,030)	Cautery**** (n = 20,816)
Temperature Zone			
1 (hottest)	21,860	2175	221
2	206,965	20866	2023
3	429,825	43481	4096
4	494,732	41462	5516
5	639,695	47843	7414
6	98,223	7796	1465
7	5,321	<400*	<100*
8 (coldest)	135	<20*	<20*
Humidity			
Moist	1,585,541	133892	17839
Dry	237,583	22990	2063
Marine	68,176	6741	833
None**	5,456	407	82

*Cells with less than 20 patients were not reported or inferred per the data use agreement.

**Temperature zones 7 and 8 are not assigned humidity zone.

***Epistaxis: ICD 9/10 codes: 784.7 and R04.0.

****Nasal Cauterization CPT codes: 30901, 30903, 30905, 30906, 31231 and 31238.

- Results:
  - 1st regression model: Effect of temperature zone and season on epistaxis.
  - Temp zone 5 – lowest odds ratio of epistaxis

TABLE II.
Relationships between demographic factors, temperature, and seasonality on pediatric epistaxis and nasal cautery*

	Epistaxis (n = 184,826) Amongst Control (n = 1,897,021)*	Nasal cautery (n = 20,816) Amongst Epistaxis (n = 184,826)**
Age (per year)	1.11 (1.11, 1.11)	1.09 (1.09, 1.09)
Female gender	0.69 (0.68, 0.7)	0.86 (0.83, 0.89)
Temperature Zone		
1 (hottest)	1.00 (reference)	1.00 (reference)
2	1.04 (0.99, 1.09)	0.93 (0.80, 1.08)
3	1.06 (1.01, 1.11)	0.88 (0.76, 1.01)
4	0.86 (0.82, 0.89)	1.23 (1.07, 1.42)
5	0.76 (0.73, 0.79)	1.36 (1.18, 1.56)
6	0.88 (0.83, 0.92)	1.62 (1.39, 1.88)
7	0.90 (0.81, 1.00)	1.72 (1.30, 2.27)
8 (coldest)	1.19 (0.67, 2.13)	1.56 (0.34, 7.21)
Season		
Winter (Jan-Mar)	1.00 (reference)	1.00 (reference)
Spring (Apr-Jun)	1.02 (1.01, 1.04)	0.96 (0.92, 1.00)
Summer (Jul-Sep)	0.48 (0.47, 0.49)	1.06 (1.02, 1.11)
Fall (Oct-Dec)	0.82 (0.81, 0.83)	1.04 (1.00, 1.09)

*Epistaxis: ICD 9/10 codes: 784.7 and R04.0.
**Nasal Cauterization CPT codes: 30901, 30903, 30905, 30906, 31231, and 31238.

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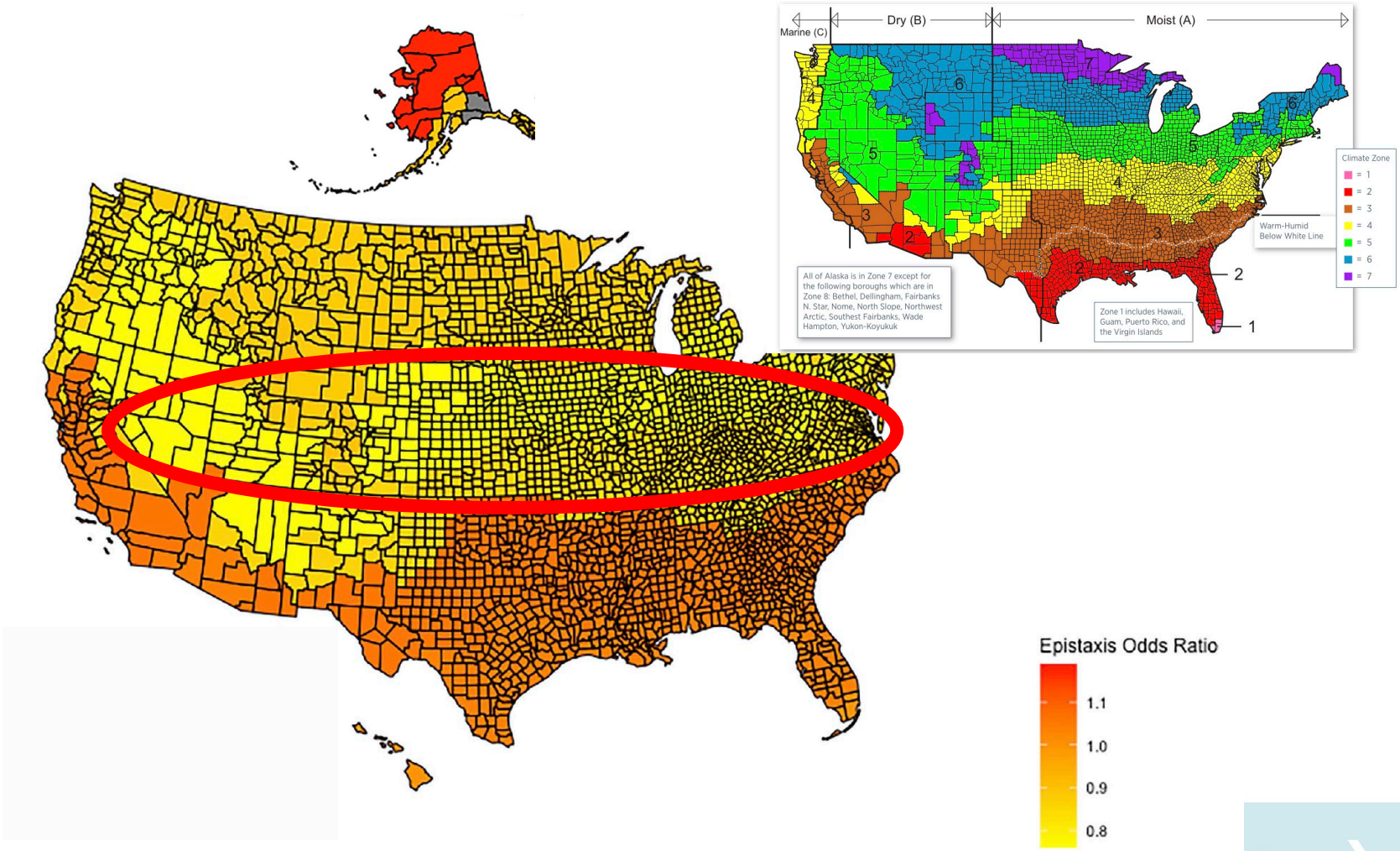

Fig. 2. Odds ratios of pediatric epistaxis by IECC-designated temperature zones.

- Results:
  - Season
  - Summer is best!

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- Results: Overall conclusion of first regression model was – "summer in moderate temperature zones was associated with lowest odds of epistaxis."

- Results:
  - 2nd regression model: Effect of temperature zone and seasons on incidence of cauterization procedures.
  - Cauterization more frequent in colder zones but also most frequent in summer.

TABLE II.
Relationships between demographic factors, temperature, and seasonality on pediatric epistaxis and nasal cautery*

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?

Environmental Risk Factors for Pediatric Epistaxis vary by Climate Zone

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- Results: Results: So why does summer have the lowest odds of epistaxis but the highest odds of having a cauterization procedure??
- Subanalysis: Univariable regressions. Evaluate association between setting of cautery, and season.

TABLE III.
Relationships Between Seasonality And Nasal Cautery Among Pediatric Epistaxis by Care Setting*.

	Office	Emergency Care	Operating Room
Winter (Dec-Feb)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Spring (Mar-May)	0.97 (0.94, 0.99)	1.02 (0.98, 1.07)	0.97 (0.87, 1.08)
Summer (Jun-Aug)	1.17 (1.14, 1.20)	0.57 (0.54, 0.59)	0.62 (0.56, 0.69)
Fall (Sep-Nov)	1.02 (1.00, 1.05)	0.81 (0.77, 0.85)	0.80 (0.72, 0.90)

*Nasal Cauterization CPT codes: 30901, 30903, 30905, 30906, 31231, and 31238.

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Eric X. Wei, MD; Allen Green, BS; Michael T. Chang, MD; Peter H. Hwang, MD; Douglas R. Sidell, MD; Z. Jason Qian, MD

- Results: What about humidity?

https://www.wonderopolis.org/wonder/what-is-humidity/

Environmental Risk Factors for Pediatric Epistaxis vary by Climate Zone

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- Results: Humidity
  - Less humidity means more epistaxis incidence in moderate temperature zones but not the case in temp extremes (zones 1&2).

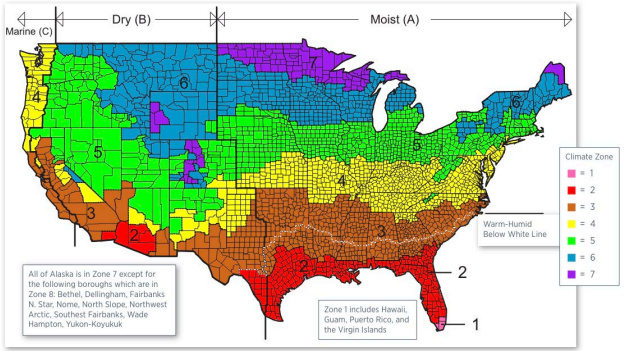

TABLE IV.
Effect of Humidity and Seasonality on Pediatric Epistaxis*.

	Zones 1–2	Zones 3–5	Zone 6	Zones 7–8
Age (per year)	1.09 (1.08, 1.09)	1.11 (1.10, 1.11)	1.15 (1.14, 1.15)	1.19 (1.17, 1.21)
Female gender	0.68 (0.66, 0.70)	0.69 (0.68, 0.70)	0.69 (0.66, 0.72)	0.70 (0.58, 0.86)
Humidity				
Moist (Zones 1–6)	1.00 (reference)	1.00 (reference)	1.00 (reference)	-
Dry (Zones 1–6)	0.96 (0.92, 1.00)	1.18 (1.16, 1.20)	1.70 (1.60, 1.81)	-
Marine (Zones 3–5)	-	1.23 (1.20, 1.26)	-	-
NA (Zones 7–8)	-	-	-	-
Season				
Winter (Dec-Feb)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Spring (Mar-May)	1.05 (1.01, 1.09)	1.03 (1.01, 1.04)	0.88 (0.83, 0.94)	1.01 (0.77, 1.32)
Summer (Jun-Aug)	0.52 (0.50, 0.54)	0.48 (0.47, 0.49)	0.42 (0.40, 0.45)	0.35 (0.26, 0.46)
Fall (Sep-Nov)	1.06 (1.02, 1.10)	0.79 (0.78, 0.80)	0.72 (0.67, 0.76)	0.61 (0.45, 0.81)

*Epistaxis: ICD 9/10 codes: 784.7 and R04.0.

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- Discussion:
  - "First study to compare the impact of meteorologic factors on pediatric epistaxis rates across a broad spectrum of climates in the United States by using the IECC climate zone classification of individual counties linked to insurance claims data."
  - Extreme temps bad
  - Moderate temps good

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- Discussion:
  - Based on these data – they "theorize that temperature extremes may lead to different mechanisms of nasal mucosal dysfunction that ultimately increase the risk of epistaxis."
  - Have temperature extremes been previously investigated in terms of mucosal dysfunction?
  - Why yes…
  - At extreme temps cilia stop beating, and mucosal sloughing occurs with return to optimal conditions
  - Similarly, in vitro studies have shown SARS-CoV-2 is more stable with decreases in air temperature relative to core body temperature, **suggesting** temperature may play a role in impairing innate immunity.

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- Limitations, questions:
  - Summer just better because of less respiratory viruses?
  - More cautery in summer
    - Because more time to bring kid in? Likely
    - Could be that "summer epistaxis" is just harder to treat conservatively but the setting data argues against this.
    - What about different temperature variations within each climate zone? Not accounted for really.
  - All privately insured kids
  - Intrinsic limitations of big databases and coding reliance
  - Retrospective
  - Don't know anterior, posterior, severity, laterality, etc.
  - Only first presentation used
  - What about other unique things to each region that aren't accounted for? (socioeconomic status, access to care, health literacy).

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- TAKE HOME POINTS:
  - Temperature extremes may be “worse” than lack of humidity for epistaxis.
  - Further investigation into temperature extremes and nasal mucosal dysfunction may provide further insight into not just epistaxis care but all things relating to nasal mucosal function.
  - As we begin to see “more frequent extreme weather events with climate change” – these findings are increasingly relevant.

The Laryngoscope

Assessing National Trends and Perceived Safety of Off-Label Ciprofloxacin-Dexamethasone Use by Pediatric Otolaryngologists

Hemali P. Shah, MD; Rema Shah, BS;
Donovan Lockwood, MD; Nan Yang, BS; Tagan Rohrbaugh, BA; Michael J. Rutter, MD;
Sarah E. Maurrasse, MD

https://complexcareathomeforchildren.com/respiratory-support/tracheostomy-care/administration-of-medication-via-tracheostomy/

- Multiple institutions
- 2023
- Laryngoscope

The Laryngoscope

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- Background
  - Why do physicians prescribe things off label?
    - Age
      - More common in pediatrics (drug trials often exclude those under 18)
    - Desire a higher or lower dose
    - Indication not covered
  - What is Ciprodex® (CPD) FDA approved for?
    - CPD is FDA-approved for the management of (1) acute otitis media (AOM) with rupture or with tympanostomy tubes and (2) acute otitis externa in patients ≥6 months.
    - CPD has been found to be effective for treating granulation in children with AOM with otorrhea through tympanostomy tubes and superior to ofloxacin for this indication.

Source: Shah BR, Lucchesi M, Amodio J, Silverberg M: *Atlas of Pediatric Emergency Medicine*: www.accessemergencymedicine.com

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Background

- Important to note, this paper never makes any distinction on which manufacturer (Alcon, Northstar, Dr. Reddy's).
- Formulations differ from different manufacturers or outside of USA?
- I have no ties (financial or otherwise) to any company or product.

Source: Shah BR, Lucchesi M, Amodio J, Silverberg M: *Atlas of Pediatric Emergency Medicine*: www.accessemergencymedicine.com
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- Background
  - Off label uses for CPD
    - Nasal surgery, choanal atresia
    - Tracheostomy management
    - Airway surgeries (endoscopic and open)
    - Given via drops or nebulized

The Laryngoscope

Assessing National Trends and Perceived Safety of Off-Label Ciprofloxacin-Dexamethasone Use by Pediatric Otolaryngologists

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- Background
  - Very little off label data
  - Many prescribers feel CPD is so effective that withholding the medication for randomized trials would be unethical.

  - Why did they do the study?
    - "Given the anecdotal safety and efficacy of CPD, we aimed to collect objective data regarding prescriber patterns, off-label indications, and accessibility of off-label CPD to establish a baseline for future research. We hope that our results will promote awareness of the utility of CPD for off-label indications and provide data to support its addition to hospital formularies for off-label indications and routes of administration."

The Laryngoscope

Assessing National Trends and Perceived Safety of Off-Label Ciprofloxacin-Dexamethasone Use by Pediatric Otolaryngologists

Hemali P. Shah, MD; Rema Shah, BS; Donovan Lockwood, MD; Nan Yang, BS; Tagan Rohrbaugh, BA; Michael J. Rutter, MD; Sarah E. Maurrasse, MD

Methods

- American Society of Pediatric Otolaryngology (ASPO) **survey**. 15 item, 3 minutes.
- Reviewed, approved, and distributed by ASPO via email to its members on two occasions, 2 months apart, from January–April 2022.
- Voluntary
- Anonymous
- No incentive noted to complete the survey (financial or otherwise)

Supplement

Ciprodex ASPO Survey

Standardized Demographics Questions from ASPO

1. How many years have you been in practice?
   - <5 years
   - 5-10 years
   - >10 years

2. Did you complete a pediatric otolaryngology fellowship?
   - Yes
   - No

3. What is the type of practice?
   - Academic Practice – Tertiary Referral Center
   - Academic Practice – Freestanding Children's Hospital
   - Private Practice – Freestanding Children's Hospital
   - Private Practice – General Hospital
   - Hospital Employed
   - Non-University Teaching Hospital
   - Government Hospital
   - Other

4. What is your geographical location of practice?
   - New England (ME, NH, VT, MA, CT, RI)
   - Mid-Atlantic (DC, MD, DE, NJ, PA, NY, VA, WV)
   - Southeast (FL, GA, SC, NC)
   - South (AR, LA, MS, AL, KY, TN)
   - Plains (ND, MN, SD, IA, NE, KS, OK, MO)
   - Great Lakes (WI, IL, IN, OH, MI)
   - Rocky Mountain (MT, ID, WY, UT, CO)
   - Southwest (AZ, NM, TX)
   - Far west (WA, OR, CA, NV)
   - Pacific (AK, HI)
   - Canada
   - Other

Ciprodex Utilization Questions

For all questions in this survey, 'off-label Ciprodex' refers to nebulized or topical Ciprodex used for indications besides otitis externa and tube otorrhea.

1. Have you ever used Ciprodex for an off-label indication (for example, airway surgery, nasal surgery, airway or nasal pathologies)
- Yes
- No

→ If 'No' to Q1, respondents will only see Q2:

2. Which of the following reasons describes why you do not use off-label Ciprodex? (select all that apply)
    - I have not heard of any off-label indications for Ciprodex
    - Not available at my practice / institution
    - I do not think it is effective
    - I do not think it is safe
    - I do not think there is enough data to support its use
    - Not applicable to my practice
    - Other, please specify: *(free text response)*

    Survey ends here for respondents who selected 'No' for Q1

→ If 'Yes' to Q1, respondents will see Q3 onwards:

3. How long have you been using off-label Ciprodex (i.e. for indications besides otitis externa)?
    - <5 years
    - 5-10 years
    - >10 years

4. Which routes have you utilized to administer off-label Ciprodex? (select all that apply)
    - Nebulized Ciprodex
    - Topical drops through a tracheostomy tube
    - Topical drops to a tracheostomy stoma
    - Topical nasal drops
    - Other, please specify: *(free text response)*

5. For which of the following indications have you used off-label Ciprodex? (select all that apply)
    - Following airway surgery
    - Tracheitis
    - Tracheal granulation
    - Stomal site granulation
    - Subglottic stenosis
    - Choanal atresia
    - Nasal congestion
    - Other, please specify: *(free text response)*

6. How often do you prescribe off-label Ciprodex each month (inpatient or outpatient)?
    - 1-5 times/month
    - 5-10 times/month
    - >10 times/month

7. What is the inpatient vs. outpatient breakdown of the patient population for which you prescribe off-label Ciprodex?

- Inpatient ___ %
- Outpatient ___%

8. How comfortable do you feel with the safety profile of off-label Ciprodex?

- Very comfortable
- Somewhat comfortable
- Somewhat uncomfortable
- Very uncomfortable

9. Do you feel the benefits of using Ciprodex off-label outweigh the risks?

- Yes
- No

10. On a scale of 1-4, how easy is it to access Ciprodex at your institution? 1=not easy at all, 4=very easy

1 2 3 4

11. To your knowledge, have any patients had adverse reactions to nebulized or topical Ciprodex?

- Yes
- No

→If 'Yes' to Q12

12. How often have you had a patient with adverse reactions to nebulized or topical Ciprodex?

- Once a week
- Once a month
- Once a year
- Once every few years

13. On a scale of 1-4, how severe were the adverse reactions? 1=not severe at all, 4=very severe

14. Please list adverse reactions to Ciprodex that patients have had.

Free text response

https://resources.pollfish.com/market-research/how-to-minimize-survey-fatigue-for-quality-research/

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- Methods
  - Stats
- Statistical analyses were performed using Rstudio v4.1.0 (Boston, MA) and GraphPad Prism v9.2.0 (San Diego, CA). Geographicregions in the United States (U.S.) were defined as West, Midwest, Northeast, South, or Southwest using U.S. Census Bureau divisions,11 and non-U.S. locations were grouped as 'Other'.

- Chi-squared and Fisher's exact tests were performed to compare categorical variables for off-label CPD users versus nonusers and based on years in practice. Chi-squared tests were performed to compare ease of access to off-label CPD across geographic regions and practice types. Comfort level and ease of access responses were categorized into binary outcomes.

- Multivariate logistic regressions were used to elucidate factors impacting comfort level and ease of access. For open-ended questions, responses were analyzed qualitatively. Common themes were identified and clarifications of responses to closed-ended questions were noted.

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- Results
  - Response rate: 26.2%
    - (Typical but not ideal)
  - 163 total responses
  - So working backward…
  - ~ 627 surveys.
  - Not sure if all ASPO members indicate willingness to do surveys
  - Consider how many otolaryngologists / surgeons who may not be ASPO members use CPD off label. Not capturing.
  - Response bias.

Results: **WHO?**

TABLE I.
Comparison of Demographic and Practice Characteristics for Pediatric Otolaryngologists Who Do and Do Not Use Off-Label Ciprofloxacin-Dexamethasone.

	No Off-Label Use $N = 7$	Yes Off-Label Use $N = 156$	p-Value
Fellowship completed, yes (%)	6 (85.7)	154 (98.7)	0.286
Type of practice (n,%)			0.947
Academic Practice—Freestanding Children's Hospital	1 (14.3)	37 (23.7)	
Academic Practice—Tertiary Referral Center	5 (71.4)	83 (53.2)	
Private Practice—Freestanding Children's Hospital	1 (14.3)	16 (10.3)	
Private Practice—General Hospital	0 (0.0)	3 (1.9)	
Hospital Employed	0 (0.0)	14 (9.0)	
Non-University Teaching Hospital	0 (0.0)	1 (0.6)	
Other	0 (0.0)	2 (1.3)	
Number of years in practice (n,%)			0.126
<5 years	0 (0.0)	31 (19.9)	
5–10 years	0 (0.0)	28 (17.9)	
>10 years	7 (100.0)	97 (62.2)	
Number of years off-label use (n,%)			-
<5 years	—	35 (22.4)	
5–10 years	—	47 (30.1)	
>10 years	—	74 (47.4)	
Geographic location			**0.004**
Northeast	2 (28.6)	32 (20.5)	
Midwest	0 (0.0)	41 (26.3)	
South	2 (28.6)	24 (15.4)	
Southwest	0 (0.0)	26 (16.7)	
West	0 (0.0)	21 (13.5)	
Canada	0 (0.0)	4 (2.5)	
Other	3 (42.9)	8 (5.1)	

Note: Bold p-Values = statistically significant ($p < 0.05$).

?

- What more do we know about these 7?

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- Results
  - Of the seven that do not use off label CPD:
  - All seven had been in practice > 10 years as we said
  - Three practice outside of USA, four within USA.
  - 4/7 stated – not enough data to support its use
  - 1/7 stated – haven't heard of off label uses
  - 2/7 stated (other reasons)
    - Difficulty accessing
    - Preference for use only after culture and sensitivities

Results: WHO? – BASED ON YEARS IN PRACTICE

TABLE II.
Overview of Demographics and Off-Label Ciprofloxacin-Dexamethasone Utilization Patterns Comparing Respondents By Number of Years in Practice.

$N = 156$	All $N = 156$	<5 years $N = 31$	5–10 years $N = 28$	>10 years $N = 97$	p-Value
Fellowship completed, yes (%)	154 (98.7)	31 (100.0)	28 (100.0)	95 (97.9)	0.540
Type of practice					0.126
Academic Practice—Freestanding Children's Hospital	37 (23.7)	6 (19.4)	7 (25.0)	24 (24.7)	
Academic Practice—Tertiary Referral Center	83 (53.2)	23 (74.2)	17 (60.7)	43 (44.3)	
Private Practice—Freestanding Children's Hospital	16 (10.2)	2 (6.5)	0 (0.0)	14 (14.4)	
Private Practice—General Hospital	3 (1.9)	0 (0.0)	1 (3.6)	2 (2.1)	
Hospital Employed	14 (9.0)	0 (0.0)	3 (10.7)	11 (11.3)	
Non-University Teaching Hospital	1 (0.7)	0 (0.0)	0 (0.0)	1 (1.0)	
Other	2 (1.3)	0 (0.0)	0 (0.0)	2 (2.1)	
Geographic location					**0.012**
Northeast	32 (20.5)	8 (25.8)	6 (21.4)	18 (18.6)	
Midwest	41 (26.2)	10 (32.3)	7 (25.0)	24 (24.7)	
South	24 (15.4)	4 (12.9)	4 (14.3)	16 (16.5)	
Southwest	26 (16.7)	3 (9.7)	0 (0.0)	23 (23.7)	
West	21 (13.5)	3 (9.7)	10 (35.7)	8 (8.2)	
Canada	4 (2.6)	2 (6.5)	0 (0.0)	2 (2.1)	
Other	8 (5.1)	1 (3.2)	1 (3.6)	6 (6.2)	
Frequency of off-label use					0.168
>10 times/month	10 (6.4)	2 (6.5)	3 (10.7)	5 (5.2)	
1–5 times/month	126 (80.8)	25 (80.6)	18 (64.3)	83 (85.6)	
5–10 times/month	20 (12.8)	4 (12.9)	7 (25.0)	9 (9.3)	
Setting of off-label use					0.657
Mean % of time inpatient (SD)	49.6 (29.7)	52.4 (27.4)	45.4 (26.3)	49.9 (31.4)	
Mean % of time outpatient (SD)	50.4 (29.7)	47.6 (27.4)	54.6 (26.3)	50.1 (31.4)	
Route of administration*					
Nebulized	95 (60.9)	27 (87.1)	20 (71.4)	48 (49.5)	**<0.001**
Topical drops through a tracheostomy tube	130 (83.3)	29 (93.5)	22 (78.6)	79 (81.4)	0.219
Topical drops to a tracheostomy stoma	111 (71.2)	30 (96.8)	21 (75.0)	60 (61.9)	**<0.001**
Topical nasal drops	134 (85.9)	28 (90.3)	26 (92.9)	80 (82.5)	0.278
Other	10 (6.4)	2 (6.5)	3 (10.7)	5 (5.2)	0.571
Indications*					
Choanal atresia	128 (82.1)	24 (77.4)	25 (89.3)	79 (81.4)	0.479
Following airway surgery	105 (67.3)	24 (77.4)	21 (75.0)	60 (61.9)	0.174
Nasal congestion	57 (36.5)	17 (54.8)	13 (46.4)	27 (27.8)	**0.012**
Stomal site granulation	108 (69.2)	30 (96.8)	21 (75.0)	57 (58.8)	**<0.001**
Subglottic stenosis	63 (40.4)	16 (51.6)	12 (42.9)	35 (36.1)	0.295
Tracheal granulation	137 (87.8)	30 (96.8)	25 (89.3)	82 (84.5)	0.187
Tracheitis	106 (67.9)	27 (87.1)	21 (75.0)	58 (59.8)	**0.012**
Other	18 (11.5)	3 (10.1)	1 (3.6)	12 (12.4)	0.294

*$N = 480$ for route of administration and $N = 731$ for indications because respondents were able to *select all that apply*.
Note: Bold p-Values = statistically significant ($p < 0.05$).
Abbreviation: SD = standard deviation.

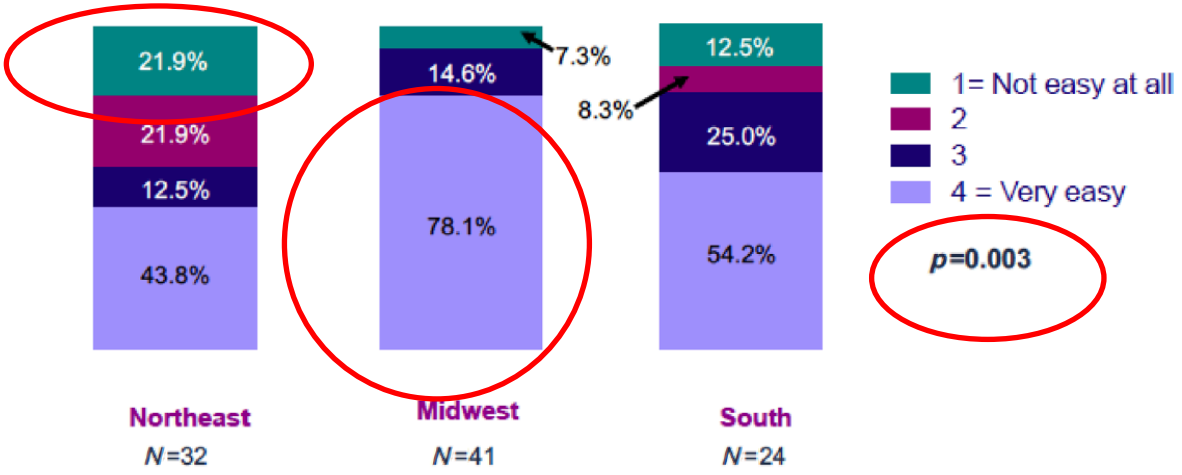
n (percent)

If you are a more juvenile responder to the survey – more likely to use it for those indications.

Older docs -less survey fatigue than younger?

Younger docs too focused on other things for the survey?

Results: **WHO HAS EASIEST ACCESS BY REGION?**



Authors postulate - given the large number of free standing "destination" children's hospitals in Midwest that do a large amount of airway surgery.

Geographic Location	Odds ratio –	p-value
Other** (Ref.)	-	-
Northeast	1.46 (0.34-6.62)	0.613
Midwest	18.79 (3.63-1.24)	**0.001**
South	5.65 (1.14-32.10)	**0.040**
Southwest	2.64 (0.55-13.60)	0.230
West	29.92 (3.55-682.00)	**0.006**

(showing higher odds of easy access)

Results: WHO HAS EASIEST ACCESS BY TYPE OF PRACTICE?

	Easy Access Odds Ratio (95% CI)	p-value
Yes Fellowship completed (ref. No)	3.88×10^{-7} (2.03×10^{-14}-2.68×10^{5})	0.988
Type of Practice (n,%)		
Other* (Ref.)	-	-
Academic Practice – Freestanding Children's Hospital	0.33 (0.02-2.75)	0.356
Academic Practice – Tertiary Referral Center	0.11 (0.01-0.64)	**0.041**
Private Practice (Freestanding Children's of General Hospital)	0.04 (0.002-0.33)	**0.009**
Number of years in practice(n,%)		
<5 years (Ref.)	-	-
5-10 years	0.60 (0.14-2.64)	0.495
>10 years	0.87 (0.28-2.57)	0.799

Harder to get in private practice

Easier in free standing children's hospitals

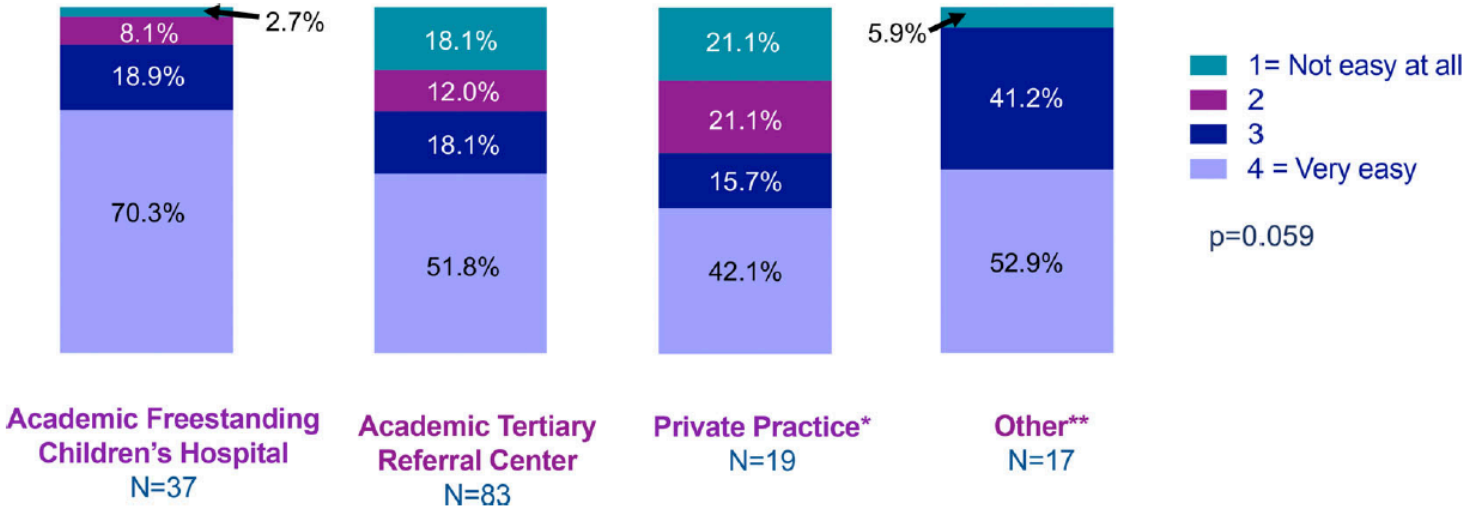


Fig. 3. Factors associated with likelihood of easy access to off-label ciprofloxacin-dexamethasone. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

The Laryngoscope

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- Results: **COMFORT LEVEL**
  - Two thirds of respondents were “Very comfortable”
  - Although 14.7% (N=23) were “very uncomfortable” with the safety profile, no adverse events reported by this group. (All used it 1-5 times per month, and all felt benefits outweighed risks.)
    - The authors response to why in discussion. Maybe they hit the wrong thing…

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- Results: **COMFORT LEVEL**
  - No respondent characteristics were associated with comfort level on multivariate analysis.

Supplementary Table 2. Factors associated with increased likelihood of comfort with off-label Ciprodex on multivariate analysis. *Other for type of practice includes respondents who selected either 'Hospital Employed', 'Non-University Teaching Hospital', 'Government Hospital' or 'Other'. **Other for geography includes respondents who selected either 'Other' or 'Canada'. Abbreviations: CI: confidence interval.

	Comfort Level Odds Ratio (95% CI)	p-value
Yes Fellowship completed (ref. No)	8.92×10^{-8} (1.01×10^{-16}-4.60×10^{9})	0.997
Type of Practice (n,%)		
Other* (Ref.)	-	-
Academic Practice – Freestanding Children's Hospital	4.16 (0.53-39.40)	0.175
Academic Practice – Tertiary Referral Center	1.00 (0.18-4.61)	0.998
Private Practice (Freestanding Children's of General Hospital)	0.48 (0.06-3.22)	0.451
Number of years in practice(n,%)		
<5 years (Ref.)	-	-

Fig. 4. Comfort level with off-label ciprofloxacin-dexamethasone across number of years in practice. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

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- Results: **COMFORT LEVEL OF RISK / BENEFIT and ADVERSE EVENTS**

TABLE III.
Perceptions of and Experiences with Safety Profile of Off-Label Ciprofloxacin-Dexamethasone.

N = 156	All *N* = 156	<5 years *N* = 31	5–10 years *N* = 28	>10 years *N* = 97	*p*-Value
Benefits outweigh risks, yes (%)	155 (99.4)	31 (100.0)	28 (100.0)	96 (99.0)	0.736
Patient experience of adverse effects, yes (%)	7 (4.5)	0 (0.0)	0 (0.0)	7 (7.2)	0.077
Frequency of adverse effects (*N* = 7)					—
Once a month	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Once a year	1 (0.7)	0 (0.0)	0 (0.0)	1 (14.3)	
Once every few years	6 (3.8)	0 (0.0)	0 (0.0)	6 (85.7)	
Severity of adverse effects (*N* = 7)					—
1 = Not severe at all	2 (1.3)	0 (0.0)	0 (0.0)	2 (28.6)	
2	3 (1.9)	0 (0.0)	0 (0.0)	3 (42.9)	
3	2 (1.3)	0 (0.0)	0 (0.0)	2 (28.6)	
4 = Very severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	

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- Results: **ADVERSE EVENTS**
  - Four had patients with cushingoid symptoms
  - One local reaction / possible allergy
  - One steroid related mental status changes
  - One neonatal patient with adrenal suppression after intranasal CPD.

Case Report

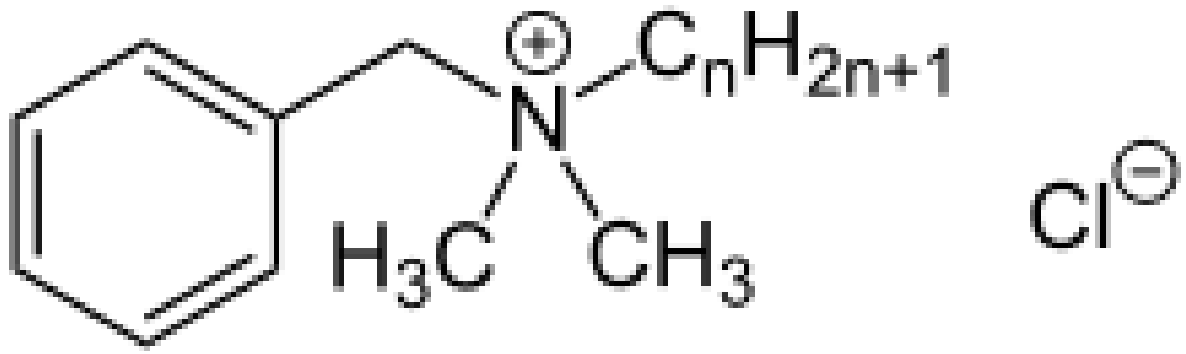
Off-Label Use of Ciprofloxacin/ Dexamethasone Drops in the Pediatric Upper Airway: Case Presentation and Review of Adverse Effects

Annals of Otology, Rhinology & Laryngology
2023, Vol. 132(5) 589–595

DOI: 10.1177/00034894221104461
journals.sagepub.com/home/aor
SAGE

Tom Ben-Dov, MD[1*], Jackie Yang, BS[2*], and Max M. April, MD[1]

- Worth review



n = 8, 10, 12, 14, 16, 18

- The preservative benzylalkonium chloride (BAC).
  - Pneumonia, UTI (?) risk
  - Brought up by the authors pharmacy
  - On their review: Concentration required to decrease FEV1 by 20% was 6.93 mg/mL. And CPD has a 0.1 mg/mL concentration of BAC, and most nebulized CPD is a 1:1 dilution with normal saline yielding a 0.05% mg/mL of BAC.
  - Zero case reports of this.

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- Conclusion / Limitations / Take home points / Discussion
  - Off label CPD usage is common and mostly safe
  - Adverse events tend to happen with very young children and prolonged usage (babies into nose – swallowing)
  - Antibiotic vs steroid component? - no discussion
  - No data on if some used it, then stopped due to AEs.
  - Self reported survey, self selective and non-response bias
  - Only ASPO members

  - Always good to stop and remember some of the limited data we have for things that we do so routinely!! Careful of group think. Yet value expert opinion for what it is and why it exists!! (expert, pattern recognition, no substitution for experience)
  - Limited data and expert opinion/experience

AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

OTO Open
2024, Vol. 8(3):e160

DOI: 10.1002/oto2.160
http://oto-open.org
WILEY

Assessing the Efficacy of Tragal Pumping in a Novel Tympanostomy Tube-Rat Model

Satoshi Hara, MD, PhD[1,2,3], Xinyu Liu, MD[1], Firasat Ali Shah, MD[1], Harumi Saeki, MD, PhD[4], Hajime Orita, MD, PhD[3,5], Airi Sakyo, MD[2,6], Takashi Anzai, MD, PhD[2], Yusuke Takata, MD, PhD[2], Kazusaku Kamiya, PhD[2], Fumihiko Matsumoto, MD, PhD[2], and Kathleen Gabrielson, DVM, PhD[1]

- June 2024
- White journal
- Hopkins & Jutendo Japan

https://www.childrensmercy.org/departments-and-clinics/otolaryngology-ear-nose-and-throat/ear-conditions/tympanic-membrane-perforation/

Original Research—Otology and Neurotology

AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

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- Background
  - Tragal pumping (TP) - a recommended adjunct to facilitate topical medication into the middle ear
  - Two studies on this prior showing TP helping - a randomized human study and an ex vivo human ear model. (1,12)
  - So why do this study?
    - Authors reason – next slide

https://www.goodrx.com/ciprodex/what-is

Original Research—Otology and Neurotology

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- Background
  - Authors reason – interested in proposing an alternative to IT injections with an ear tube and tragal pumping
  - Intratympanic injection recommendations
    - up to 4 sessions within 2 weeks

Practice Guideline > Otolaryngol Head Neck Surg. 2019 Aug;161(1_suppl):S1-S45.
doi: 10.1177/0194599819859885.

Clinical
(Update

Practice Guideline > Otolaryngol Head Neck Surg. 2020 Apr;162(2_suppl):S1-S55.
doi: 10.1177/0194599820909438.

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Affiliations +
PMID: 313693

Clinical Practice Guideline: Ménière's Disease

Gregory J Basura [1], Meredith E Adams [2], Ashkan Monfared [3], Seth R Schwartz [4], Patrick J Antonelli [5], Robert Burkard [6], Matthew L Bush [7], Julie Bykowski [8], Maria Colandrea [9], Jennifer Derebery [10], Elizabeth A Kelly [11], Kevin A Kerber [1], Charles F Koopman [12], Amy Angie Kuch [13], Evie Marcolini [14], Brian J McKinnon [15], Michael J Ruckenstein [16], Carla V Valenzuela [17], Alexis Vosooney [18], Sandra A Walsh [19], Lorraine C Nnacheta [20], Nui Dhepyasuwan [20], Erin M Buchanan [20]

Original Research—Otology and Neurotology

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2024, Vol. 8(3):e160

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- Background
  - Mostly irrelevant to my practice but may impact yours - will let you decide
  - I was more interested in review of their data to justify telling families to tragal pump or not.
    - Why?
    - Many families – ear drops are probably harder than we think. Should we tell them to tragal pump or not?

Original Research—Otology and Neurotology

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Background

- Need to talk about 2 previous studies.

- Kaiser – Oakland.
- 2011
- 24 kids
- Time of tube placement
- 1.27mm ID fluoroplastic tube placed
- Floxin with methylene blue in both ears
- 4 tragal pumps on 1 ear, no pumps on other ear
- 2nd blinded operator evaluated promontory mucosa for staining.
- Yes or no eval for staining

Original Research—General Otolaryngology

AMERICAN ACADEMY OF OTOLARYNGOLOGY–HEAD AND NECK SURGERY FOUNDATION

Otolaryngology–Head and Neck Surgery
144(6) 891–893

DOI: 10.1177/0194599811399711
http://otojournal.org
SAGE

Assessing the Efficacy of Tragal Pumping: A Randomized Controlled Trial

Nathan H. Boyd, MD[1], and Joshua A. Gottschall, MD[1]

Middle ear penetration of otic drops was present in 33% (8/24) of control ears and in 75% (18/24) of experimental ears, resulting in a statistically significant difference (P = .0094).

Original Research—Otology and Neurotology

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- Background
  - 2nd study to discuss – the ex vivo one

- MCG 2000
- "Ex vivo" "in vitro"
- Human head model
- Fiberglass, acrylic, epoxy
- 5 solutions (tap water, soapy water, tobradex, cortisporin, cipro)
- Ohmeter
- Resistance change noted if liquid in middle ear – measured via electrodes

Otolaryngol Head Neck Surg. 2000 Mar;122(3):330-3. doi: 10.1016/S0194-5998(00)70042-8.

Tympanostomy tubes and otic suspensions: do they reach the middle ear space?

R L Hebert 2nd [1], M L Vick, G E King, J P Bent 3rd

Without the use of slight tragal pressure, Cortisporin, TobraDex, and Cipro drops did not consistently pass through the TT (0/20, 1/25, 1/25). By placing the drops with the addition of tragal pressure, a statistically significant difference was obtained for each solution (20/20, 20/20, and 20/20, respectively [P < 0.0001]). We conclude that with a clean external auditory canal, patent TT, and no middle ear fluid, medicated otic suspensions enter the middle ear only when combined with slight tragal pressure.

Original Research—Otology and Neurotology

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- Background
  - Other than those 2 studies – that's it! So this was 3rd ever study on this.
  - Many families – ear drops are probably harder than we think. Should we tell them to tragal pump or not?
  - As we know….
    - Kids are nuts!

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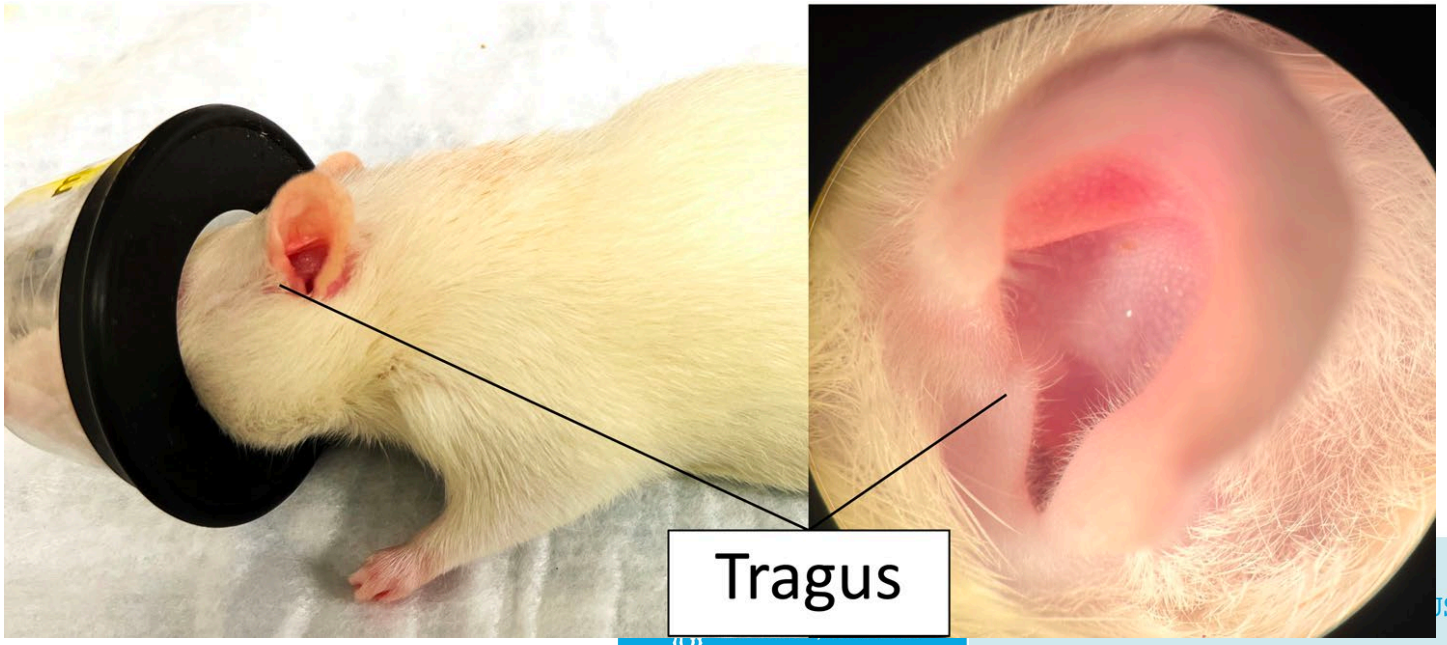
- Methods
  - Sprague-Dawley rats
  - 5 male, 5 female
  - 6-8 months of age
  - Standard lab rat conditions



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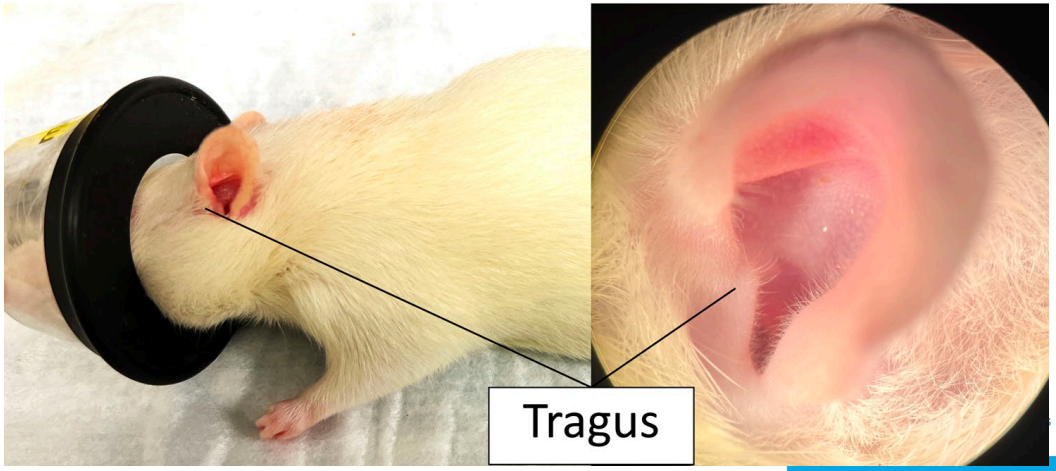
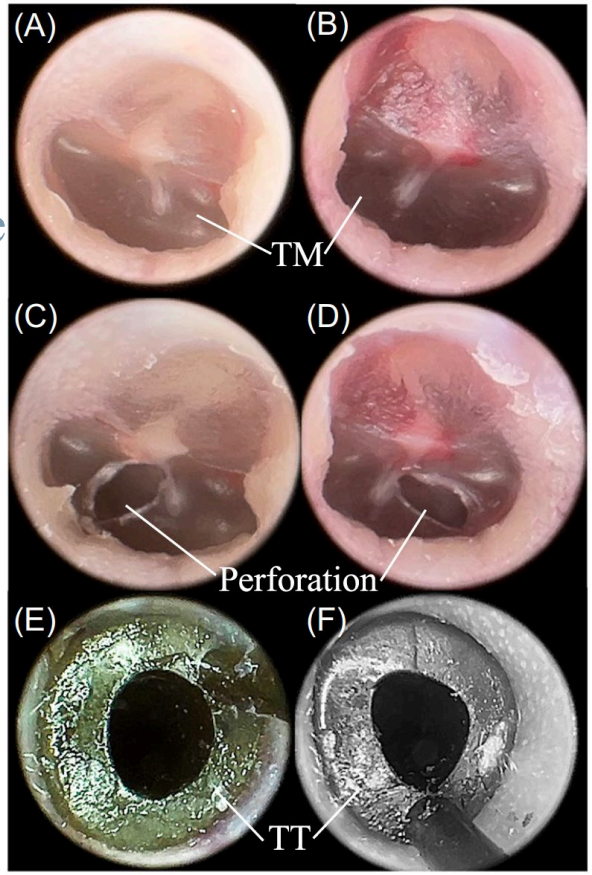
Methods

- Anesthesia – isoflurane
  - reflex-to-toe pinch, respiratory rate, body temperature
- Both ears examined with microscope and endoscope
- Placed tubes (Silicone Shepard Ventilation Tube, 1026025, ID: 1.14 mm; Medtronic) (come back to this in the discussion)





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Takashi Anzai, MD, PhD[2], Yusuke Tak
Kazusaku Kamiya, PhD[2], Fumihiko Ma
Kathleen Gabrielson, DVM, PhD[1]

- Methods
  - First – a little pilot experiment
  - After tubes inserted
  - Temporal bone harvested
  - Microscopic analysis showed that the tubes were correctly placed in the tympanic membrane (Figure 3).

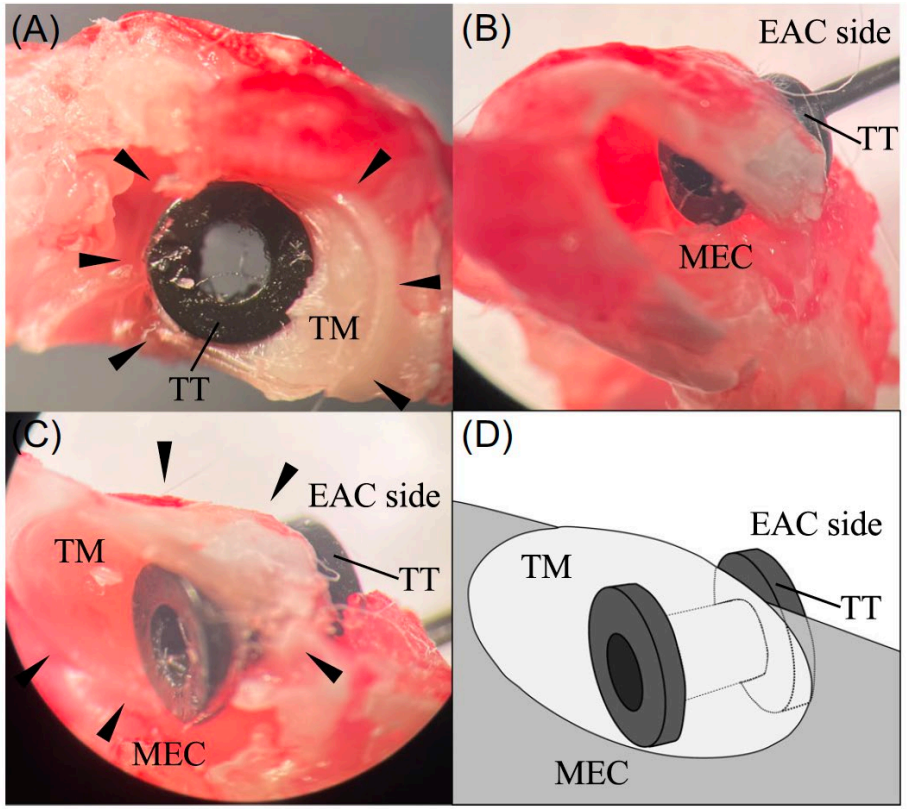

Figure 3. Microscopic images and an illustration of a temporal bone for the confirmation of the placement of tympanostomy tube insertion. (A) Lateral view of the temporal bone from the EAC side. The tympanostomy tube was on the tympanic membrane. (B, C) After opening the middle ear cavity, the tympanostomy tube passed through the tympanic membrane. One flange of the tube was in EAC, and the other one was in MEC. (D) An illustration of (C). EAC, external auditory canal; MEC, middle ear cavity; TM, tympanic membrane; TT, tympanostomy tube.

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- Methods
  - Drop procedure
    - Rats laid in lateral position
    - 100 uL solution placed into EAC w/ 22G catheter connected to a 1mL syringe - application done under microscopic review.
      - Volume used based off previous studies for rats
    - Green Davidson® tissue marking dye (1163-1; Bradley Products Inc) was diluted (1:2) with distilled water and used as eardrops.
      - This tissue dye used based on ability to tolerate the sectioning. Discuss in discussion – methylene blue washed out for example.
    - Tragus gently pushed for 1 minute in experimental ears, and not done in control ears.
    - 30 minutes after administration. Solution removed. Tubes then removed.
    - Euthanized.
    - 5 TP left ears and 5 TP right ears
    - NOTE: For a given rat – TP ear done first, then control ear.

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- Results
  - 2 outcome measures
  - Staining GRADE
  - Staining LEVEL

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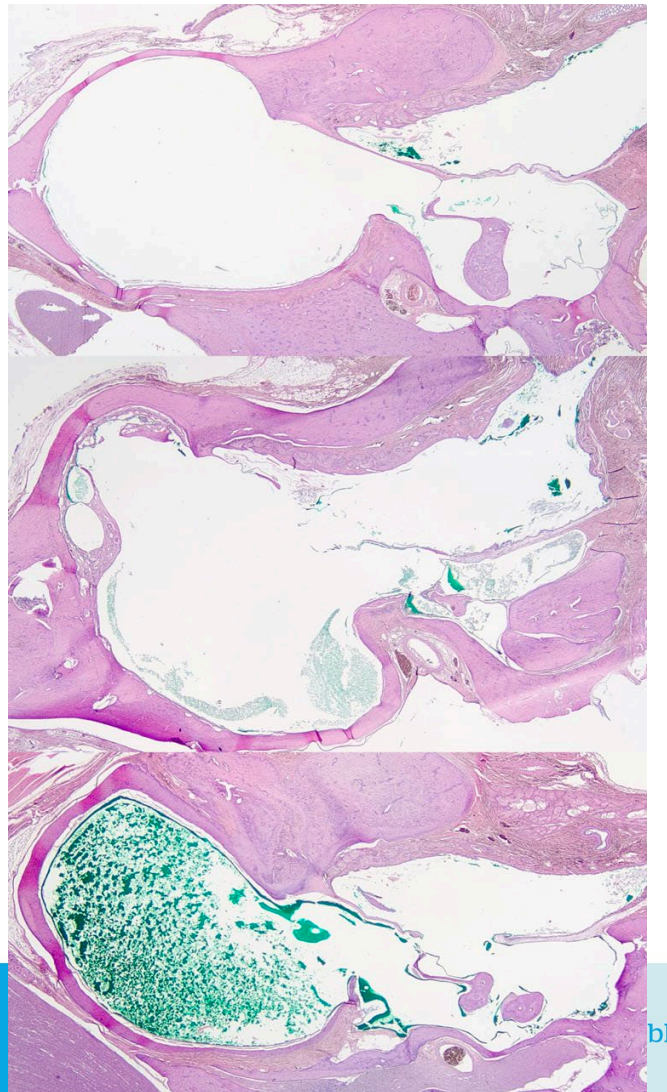
- Results
  - STAINING GRADE (by blinded pathologist)
    - Grade 1 → (less than 5% middle ear stained)
    - Grade 2 → (5%-40% stained)
    - Grade 3→ (over 40% stained)



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- Results
  - STAINING GRADE

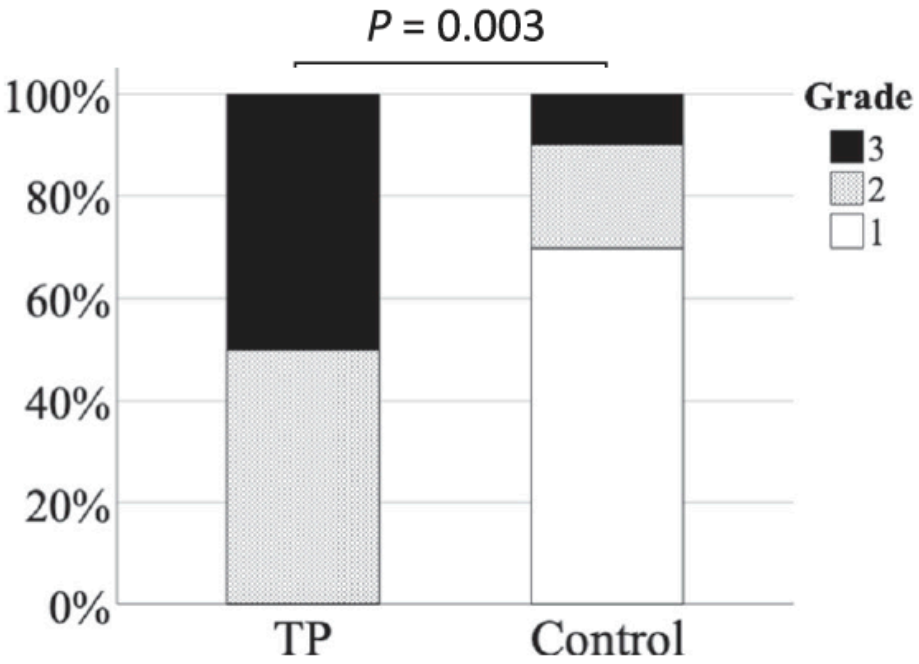

Figure 6. The distribution of the staining grades of the middle ear cavity in the TP and control ears. TP, tragal pumping.

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- Results
  - STAINING LEVEL
    - An attempt to replace a blinded pathologist's subjectivity with an objective measure.
    - Image J software methodologies
    - Dyed vs undyed area.
    - Staining level (%) – (dyed area)/(dyed area + undyed area)

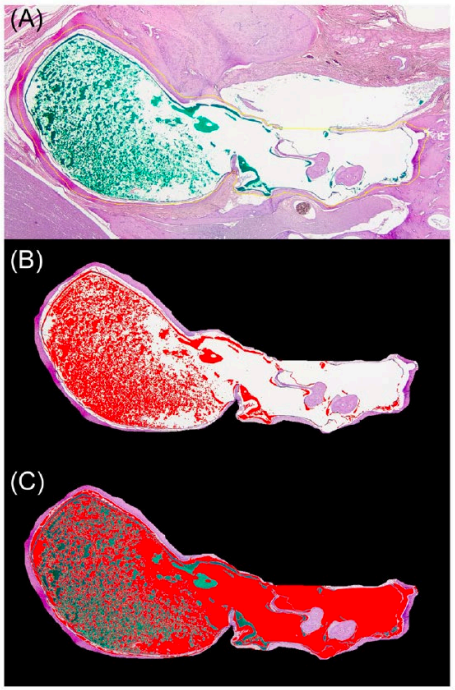

Figure 5. Representative images of temporal bone sections during the image analysis by a blinded scorer using Image J software. (A) Process of cropping middle ear cavity. The yellow line is a cropping line. (B) Process of selecting the green dyed area in the middle ear cavity specifically. The red area in this picture is the selected area. (C) Process of selecting the white undyed area in the middle ear cavity specifically. The red area in this picture is the selected area.

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- Results
  - STAINING LEVEL

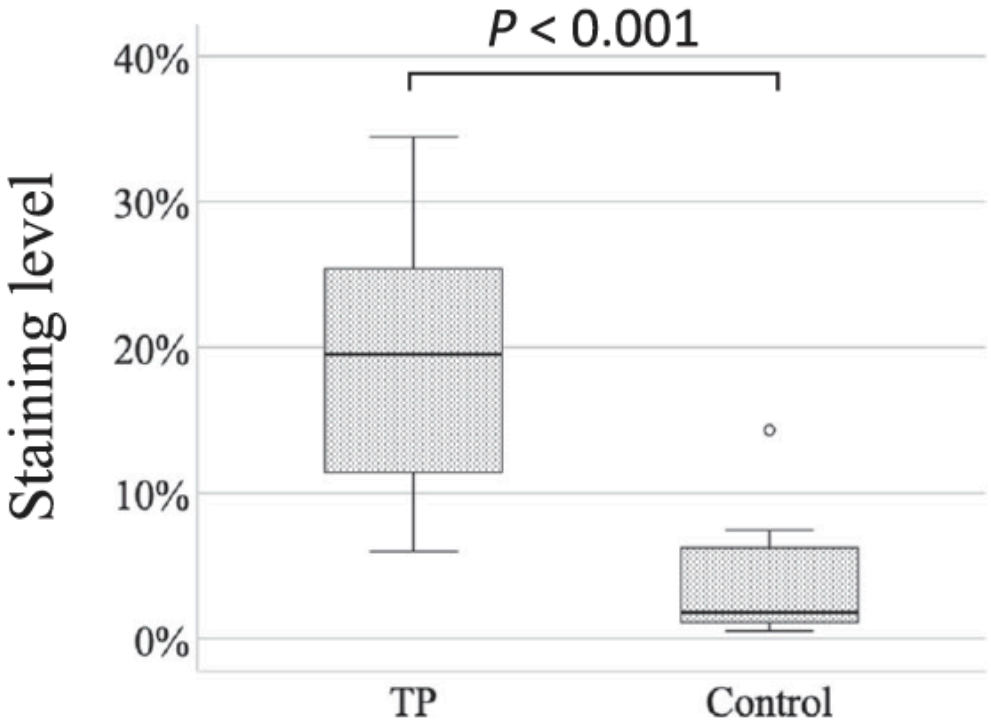

Figure 7. The staining level of the middle ear cavity in the TP and control ears. TP, tragal pumping.

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- Results
  - STAINING LEVEL and STAINING GRADE correlation

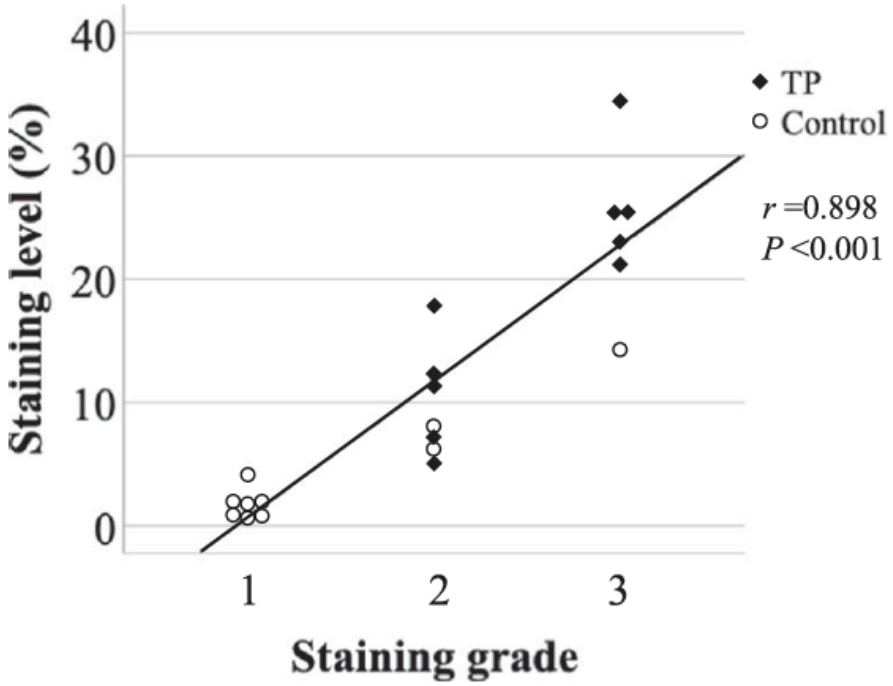

Figure 8. The staining grade and the staining level of the middle ear cavity. Pearson correlation, $r = .898$, $P < .001$. TP, tragal pumping.

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- Discussion
  - Rats – under anesthesia for ear drops. Kids aren't
  - Tube size relative to TM and EAC
  - EAC volume important. Boyles law.
  - No formal pressure measurement to correlate penetration with.
  - Viscosity/surface tension/volume considerations.
  - Did not test actual oto-topicals we use.
  - Often there is some otorrhea in the canal already for kids– could affect viscosity and penetration
  - Amount of stuff to be stained in the middle ear differ from humans? Matter?
  - Did not clarify how many times pumped. (Slow and hard, fast and wimpy?)
  - They say - Don't think the order of ears mattered because it is not looking at degree of staining just staining or not. (i.e. not like immunohistochemistry) – I'm not so sure.

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- Take home message
  - Based on this and the 2 other studies that exist – tragal pumping does seem to be useful.
  - How long and hard to pump is hard to say
  - Some will do what they will do regardless
  - How will you counsel your sensory families?
  - Remember – no information here on whether getting the solution (clinically – this would be quinolone drop usually) into middle ear actually has a clinical benefit. But it is related. How much of our data on topical treatment is accurate / causal for antibiotic drop? (i.e. how many cases of purulent otorrhea, never got the drops in, family did a poor job of drops, no tragal pumping, kid wouldn't tolerate it, whatever - and it eventually resolved regardless – in many immunocompetent kids – this is the case.)

JAMA Pediatrics | Original Investigation

Effectiveness of Intranasal Mometasone Furoate vs Saline for Sleep-Disordered Breathing in Children
A Randomized Clinical Trial

Alice Baker, MBBS; Anneke Grobler, PhD; Karen Davies, MBBCh; Amanda Griffiths, MBBS; Harriet Hiscock, MD; Haytham Kubba, MD; Rachel L. Peters, PhD; Sarath Ranganathan, PhD; Joanne Rimmer, MA; Elizabeth Rose, MBBS; Katherine Rowe, MBBS; Catherine M. Simpson, PhD; Andrew Davidson, MD; Gillian Nixon, MD; Kirsten P. Perrett, PhD

https://www.goodrx.com/ciprodex/what-is