of treatment will last, whether refresher courses will be necessary, and whether this treatment will be cost-effective and reimbursed by third-party payers (since behavioral intervention requires multiple teaching sessions conducted by a specialist in this field). It seems very reasonable to consider biofeedback training for motivated patients who prefer not to take medications for the long term or who are unable to tolerate them.

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Aspirin and the Risk of Hemorrhagic Stroke

Jiang H, Whelton PK, Vu B, Klag MJ. Aspirin and risk of hemorrhagic stroke: a meta-analysis of randomized controlled trials. JAMA 1998; 280:1930-5.

Clinical question **What is the risk of hemorrhagic stroke associated with aspirin treatment?**

Background Aspirin is widely used to reduce the risk of myocardial infarction and ischemic stroke. While several studies have shown an increase in the risk of hemorrhagic stroke among aspirin users, none had sufficient statistical power to provide definitive results.

Population studied Trials from North America, Europe, the United Kingdom, and Australia were included in this meta-analysis. Patients were predominantly men (86%) and white (99%), with an average age of 59 years. Fourteen of the 16 trials included only patients with preexisting cardiovascular or cerebrovascular disease. The 2 remaining trials, which studied healthy white men, included as many participants as the other 14 trials combined.

Study design and validity This study was a meta-analysis, combining patient data from randomized controlled trials in which participants were treated with aspirin, a placebo, or nothing. Patients in the treatment groups of these trials took only aspirin or placebo for at least 1 month. Sixteen trials with 55,462 participants were included in this meta-analysis. The mean dose of aspirin was 273 mg per day (range = 75 - 1500 mg/day) and the mean duration of treatment was 37 months. A total of 108 hemorrhagic stroke cases occurred in 13 of the 16 trials. No hemorrhagic strokes were reported in the 3 remaining trials. Information on country of origin, sample size, duration of study, study design, aspirin dosage, participant characteristics, and outcomes was independently abstracted by 2 of the authors using a standardized protocol.

Numerous trials have compared aspirin treatment with treatments using other antiplatelet or anticoagulant medications, and others have studied a combination of aspirin therapy with one of these medications compared with a control. By choosing to include only studies that met the above criteria, the authors were able to isolate the effect of aspirin on the risk of hemorrhagic stroke. In addition, the combination of randomized studies and meta-analysis techniques allowed the authors to find differences with enough statistical strength to provide definitive results regarding that risk, something that had not been possible with the individual trials.

Outcomes measured The primary outcome was the likelihood of different types of stroke during treatment. In addition, the authors assessed the overall likelihood of stroke and myocardial infarction, cardiovascular disease mortality, and all-cause mortality that occurred during treatment.

Results The total number of strokes was reduced by 31 events per 10,000 persons (95% confidence interval [CI], 5 - 57; $P = .02$). A total of 322 people had to be treated for 1 to benefit (number needed to treat [NNT] = 322). Aspirin use was associated with an increase in the absolute risk of hemorrhagic stroke of 12 events per 10,000 persons (95% CI, 5 - 20; $P < .001$; number needed to harm [NNH] = 833). However, aspirin reduced the likelihood of ischemic stroke by 39 events per 10,000 persons (95% CI, 17 - 61; $P < .001$; NNT = 256). Neither patient characteristics nor study design influenced the absolute risk.

Overall, aspirin use reduced all-cause mortality by 120 per 10,000 persons (95% CI, 77 - 162; $P < .001$; NNT = 83). Cardiovascular deaths were decreased by 97 per 10,000 (95% CI, 59 - 135; $P < .001$; NNT = 103). The incidence of myocardial infarction was reduced by 137 events per 10,000 persons (95% CI, 107 - 167; $P < .001$; NNT = 73), and fatal myocardial infarction rates were reduced by 37 events per 10,000 persons (95% CI, 16 - 55; $P < .001$, NNT = 270).

Recommendations for clinical practice **This meta-analysis quantifies the risk of hemorrhagic stroke associated with aspirin therapy. The NNH of patients treated with aspirin to have 1 event of hemorrhagic stroke is 833. Although this is not an insignificant number considering the potentially catastrophic implications of hemorrhagic stroke, it is much higher than the NNT with aspirin to prevent the complications of cardiovascular disease. Therefore, for patients for whom aspirin is being prescribed for secondary prevention or for those with multiple risk factors, the benefits of aspirin therapy outweigh the risks. For low-risk individuals, including men and women younger than 50 years without evidence of heart disease, aspirin**

therapy might cause more harm than good and should not be routinely prescribed.

Further studies are needed that address the benefits and risks of aspirin use in women, nonwhite people, and those at increased risk for hemorrhagic stroke.

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Intranasal Steroids or Antihistamines for Allergic Rhinitis?

Weiner JM, Abramson MJ, Puy RM. Intranasal corticosteroids versus oral H_1 receptor antagonists in allergic rhinitis: systematic review of randomized controlled trials. Br Med J 1998; 317:1624-9.

Clinical question **Are intranasal corticosteroids more effective than oral antihistamines for the treatment of allergic rhinitis?**

Background Treatment for allergic rhinitis is a common reason for primary care visits. While intranasal corticosteroids are generally considered more effective than oral antihistamines for nasal symptoms, oral antihistamines are still more frequently prescribed (see the list at www.rxlist.com/top200.htm). Intranasal corticosteroids are also thought to be less effective for comorbid ocular symptoms.

Population studied In this meta-analysis, the authors identified 16 trials with 2267 patients that compare one of several intranasal corticosteroids to any oral antihistamine for the treatment of nasal, ocular, and global symptoms of allergic rhinitis. No information is given regarding the settings of the original studies.

Study design and validity This meta-analysis of randomized controlled trials is well done. The question is clearly defined, and it addresses a problem that is common in primary care. The proposed intervention (steroid nasal sprays) is feasible. The search strategy is thorough, using 2 separate databases (MEDLINE and the European EMBASE). Although citations in review articles and abstracts from conferences were investigated, no mention is made of a search for unpublished studies. The authors clearly define their inclusion and exclusion criteria for the review. The quality of the included studies is assessed and classified according to the criteria of the Cochrane Collaboration. Two reviewers performed this quality assessment independently. Heterogeneity of results was found for several end points (significant variation in outcomes between studies), and the authors appropriately conducted sensitivity and subgroup analyses in an attempt to explain this.

Outcomes measured The effectiveness of treatment on the patient-oriented outcomes of nasal symptoms (blockage, discharge, sneezing, itch, postnasal drip, total nasal symptom score), eye symptoms, and systemic or global symptoms was reported.

Results Intranasal steroids were superior to oral antihistamines for all patient-oriented nasal symptom outcomes. Results were reported as the standard mean difference (SMD) in symptom scores, a statistical method allowing scores from different survey instruments and scales to be pooled. The SMD represents the mean difference in symptom score for patients receiving intranasal steroids compared with patients receiving oral antihistamines, expressed in units of the standard deviations of those scores. Fourteen trials considered nasal blockage, discharge, and sneezing, giving SMDs of -0.63, (95% confidence interval [CI], -0.73 to -0.53), -0.50 (95% CI, -0.60 to -0.40), and -0.49 (95% CI, -0.59 to -0.39), respectively. In the 11 trials considering nasal itch, intranasal steroids resulted in an SMD of -0.38 (95% CI, -0.49 to -0.21). Postnasal drip was studied in 2 trials, showing an SMD of -0.238 (-0.42 to -0.06.) Nine studies reported a total nasal symptom score, with an SMD -0.42 (95% CI, -0.53 to -0.32). Only one trial studied nasal resistance, and it found no difference between treatments.

Eye symptoms were reported by 11 studies. There was no statistically significant difference between intranasal steroids and oral antihistamines, with an SMD of -0.04 (95% CI, -0.16 to 0.07). Global ratings were reported by 2 studies. The results are expressed as the odds for deterioration or no change in symptoms in the intranasal steroid group versus the oral antihistamine group. This odds ratio is 0.26 (95% CI, 0.08 - 0.8) and favors intranasal steroids. Heterogeneity of results was found only for the symptoms of sneezing, total nasal symptoms score, and ocular symptoms. Subgroup analysis showed that this heterogeneity was probably not due to the use of different steroids and antihistamines between the trials.

Recommendations for clinical practice **This meta-analysis supports the generally held belief that intranasal corticosteroids are more effective than oral antihistamines for the common nasal symptoms of allergic rhinitis. However, the lack of difference found for ocular symptoms suggests that our traditional regard of antihistamines as the superior treatment for these symptoms may be wrong. Given the higher effectiveness, lower cost, and general bias toward topical or local treatments over systemic ones, we should use**