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Antibiotics, Acne, and Upper Respiratory Tract Infections

Editor's note: About two million people per year in the U.S have acne severe enough to require treatment with antibiotics. Treatment frequently lasts for more than six months, prompting concerns about antibiotic resistance and other possible consequences of long-term antibiotic use, such as increased susceptibility to infections. This Issue Brief summarizes a large study that evaluates the risk for upper respiratory and urinary tract infections among adolescents and young adults treated with antibiotics for acne.

Risks of long-term antibiotic use suspected, but not actually known

Despite concern about the ramifications of long-term antibiotic use, few studies have been conducted on populations of patients who have actually been exposed to antibiotics for long periods. Acne represents a model of a disease in which to study this issue, because long-term antibiotic use (greater than six weeks) is standard and appropriate therapy.

- Topical and oral antibiotics are frequently used to treat acne. The most common antibiotics prescribed are tetracyclines, erythromycin, and clindamycin.
- Previously, Margolis and colleagues showed that antibiotic therapy for acne increased the chances that a young adult will harbor group A streptococci, an organism associated with pharyngitis (sore throat). In a small study, they found that nearly 35% of acne patients on antibiotic therapy had group A strep in their upper airway, and nearly 85% of the organisms were resistant to tetracyclines. In comparison, about 19% of acne patient not using antibiotics had group A strep organisms, 20% of which were resistant to tetracyclines. However, these patients had no symptoms of a sore throat or respiratory illness and so the clinical implications of these findings are not clear.

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- The question remains whether long-term antibiotic use results in an increase in upper respiratory tract infections (URIs). The vast majority of URIs are viral, not bacterial, although some researchers suspect that antibiotics may indirectly increase an individual's susceptibility to viral infections.

Study tracks rate of infections in patients with acne

To determine whether long-term antibiotic use for acne results in increased risk for infections, Margolis and colleagues used the General Practitioner Research Database (GPRD), a large medical records database in the United Kingdom, to identify a group of patients ages 15-35 who had been diagnosed with acne between 1987 and 2001.

- The researchers classified acne patients as antibiotic users if the database indicated use of oral or topical antibiotics for more than six weeks, and classified all other acne patients as non-users. All patients were followed up in the database for 12 months after being identified.
- The researchers compared the incidence of URIs (such as pharyngitis, tonsillitis and laryngitis) in antibiotic users and non-users. To test whether more frequent diagnosis of URI might be linked to more frequent doctor visits by users, they also compared the incidence of urinary tract infections in each group. Urinary tract infections are not likely to be affected by the topical antibiotics used to treat acne.
- As a further test of whether a URI diagnosis is related to the frequency of office visits, the researchers tracked URIs in a similar group of patients with hypertension rather than acne. These patients also have frequent office visits, but should be at no increased risk for URIs.

Acne patients using antibiotics had twice the risk of URI within a year as non-antibiotic users

The analysis confirmed that acne patients on long-term antibiotics have more upper respiratory tract infections, even after accounting for factors such as age, sex, and frequency of office visits for acne.

- Of 118,496 individuals with acne, 84,977 (71.7%) received topical or oral antibiotics for more than six weeks and 33,519 (28.3%) did not. Almost 93% of patients on antibiotics used a combination of topical and oral agents.
 - Within the first year of observation, 18,281 (15.4%) of the patients with acne had at least one URI. Antibiotic users were twice as likely to be diagnosed with a URI as non-users, a risk that was present whether the patient used topical antibiotics, oral antibiotics, or both.
 - As expected, there was no difference between antibiotic users and non-users in the rate of urinary tract infections.
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- Hypertensive patients and acne patients not on antibiotics had similar rates of URIs, again suggesting that health care-seeking behavior did not explain the higher rate of URI in acne antibiotic users.

Long-term antibiotics may have systemic effects

The reasons that acne antibiotic users might be at increased risk for URI are not clear. As noted earlier, most URIs are caused by viruses, which are not directly affected by antibiotics used to treat acne. The researchers pose a number of possible explanations for an increased risk for URI in this population, including:

- The frequency of URIs of bacterial origin may be higher than previous suspected, especially in this age group.
- Some URIs could have multiple origins, in that having one organism (bacteria or virus) may increase the chances of infection by another organism. In this case, patients harboring group A strep might be more vulnerable to URIs of viral origin.
- Long-term antibiotics could cause immune system changes that could lead to increased susceptibility to certain viral infections.

POLICY IMPLICATIONS

This study documents, for the first time, that antibiotic use in acne is associated with an increased risk of URI. Prolonged use of antibiotics may cause social harm related to cost and the development of antibiotic-resistant organisms and may cause individual harm to patients receiving prolonged courses of antibiotics. Further studies are needed to confirm these findings, and to determine the mechanisms for the increased risk.

- At this point, these findings do not warrant a change in clinical practice. If the risk for URIs is confirmed, patients and practitioners will need to balance the risk of these infections with the benefits that patients with acne receive from antibiotics.
 - Further research is needed to address important clinical questions, such whether the dosages of antibiotics are linked to the risk, number, or severity of infections.
 - This study underscores the message that antibiotics should be used only when necessary, and for only as long as necessary.
 - Acne patients, many of whom use a combination of topical and systemic antibiotics for long periods, make ideal subjects for studies of the long-term effects of antibiotics and bacterial drug resistance.
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This Issue Brief is based on the following article: D.J. Margolis, W.P. Bowe, O. Hoffstad, J.A. Berlin. Antibiotic treatment of acne may be associated with upper respiratory tract infections. Archives of Dermatology, September 2005, vol. 141, pp. 1132-1136. See also R.M. Levy, E.Y. Huang, D. Roling, J.J. Leyden, D.J. Margolis. Effect of antibiotics on the oropharyngeal flora in patients with acne. Archives of Dermatology, April 2003, vol. 139, pp. 467-471.

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