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The Mental Side Effect of Antibiotics

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Abstract:
This report is about the mental side effects of antibiotics, showcasing the classes of drugs that might have psychiatric effect, their proposed mechanism and some possible risk factors.

Introduction:
Antibiotics are among the most frequently prescribed medications in modern medicine. Antibiotics cure disease by killing or injuring bacteria. The first antibiotic was penicillin, discovered accidentally from a mold culture. Today, over 100 different antibiotics are available to cure minor, and life-threatening infections. Although antibiotics are useful in a wide variety of infections, it is important to realize that antibiotics only treat bacterial infections. Antibiotics are useless against viral infections (for example, the common cold) and fungal infections (such as ringworm). Your doctor can best determine if an antibiotic is right for your condition. Antibiotics may have side effects. Some of the more common side effects may include:

* Soft stool or diarrhea
* Mild stomach upset

You should notify your doctor if you have any of the following side effects:

* Vomiting
* Severe watery diarrhea with abdominal cramps
* Allergic reactions
* Rash
* White patches on tongue

Discussion:
Antibiotics can cause symptoms of anxiety like gastrointestinal issues and even dizziness. Some medicines may cause depression and suicidal thoughts as well, as mentioned on their labels as possible side effects. The exact mechanisms by which antimicrobials produce altered mental status are largely unknown. Antimicrobials may have direct and secondary effects on the CNS. Antimicrobials may directly alter CNS function through alteration of neurotransmission such as gamma-aminobutyric acid (GABA) antagonism by fluoroquinolones, cephalosporins, and penicillins.

In addition, antimicrobials may interact with concurrent medications and produce CNS effects. Examples include serotonergic syndrome with linezolid and other serotonergic drugs or antimicrobial inhibition of cytochrome P450 enzymes, resulting in accumulation of other CNS-acting medications.
*some examples of drugs with mental side effects:

**Fluoroquinolones**
A recent US Food and Drug Administration (FDA) safety alert (and subsequent label revision) cautions against the use of fluoroquinolones for common infections when other alternatives are available, owing to potential adverse effects, including CNS toxicity. The FDA recommends that patients watch for signs and symptoms of confusion or hallucinations.

**Beta-Lactams**
Beta-lactams differ in their propensity to cause mental status changes, possibly because of side chain differences. Neurotoxicity is more likely with beta-lactams with more basic side chains, owing to increased GABA receptor binding. This difference may explain why meropenem is less neurotoxic than imipenem, which has a more basic side chain. Differences in neurotoxicity may guide treatment choices for patients with increased neurotoxic risk, such as seizure disorders. For example, ceftazidime and meropenem are less neurotoxic than cefepime and imipenem.

**Cephalosporins**
One retrospective study of 100 patients treated with intravenous cefepime in the intensive care unit between 2009 and 2011 found that 15% experienced cefepime-associated neurotoxicity. These patients were less likely to have appropriate renal dose adjustments and more likely to have a history of chronic kidney disease. Although cephalosporin neurotoxicity is more common with cefepime than other cephalosporins, such as ceftriaxone, it is less likely to be identified, and delayed diagnosis is common.

**Metronidazole**
The combination of metronidazole and disulfiram has been linked to psychosis; this is thought to be due to the coinhibition of aldehyde dehydrogenase. In a study of 58 men receiving disulfiram for chronic alcoholism, 20% who were also given metronidazole developed an acute psychosis/confusional state. Metronidazole neurologic toxicity appears to be associated with increasing cumulative doses and exposures. Because of the risk for neurotoxicity with repeat exposures to metronidazole, limiting its duration of use is recommended.

**Oxazolidinones (Linezolid)**
Because linezolid inhibits monoamine oxidase A and B, concomitant use with medications that increase serotonin levels can lead to serotonin syndrome and subsequent adverse neurologic effects. Toxicities due to serotonin syndrome can range from tremors to altered mental status, coma, or death. Up to 25% of infectious disease practitioners have reported observing serotonin syndrome when linezolid is administered concomitantly with selective serotonin reuptake inhibitors or serotonin/norepinephrine reuptake inhibitors.

In 2011, the FDA issued a warning about CNS reactions with linezolid, and later strengthened this alert to say that "linezolid generally should not be given to patients taking serotonergic drugs" although avoidance of combination use or use without a "washout" period is often problematic in the clinical setting.

*Possible risk factors:

1- Pre existing neurological disease

2- High doses

3- Age

4- Renal impairment
**Conclusion:**
If altered mental status related to antimicrobials is suspected, management may involve a decrease in the drug dose, selection of another antimicrobial, or discontinuation if possible. In most cases, discontinuing the offending agent will lead to resolution of symptoms within 48 hours.

**References:**