

## Challenges Pertaining to Adverse Effects of Drugs

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### Introduction

Adverse effects are the leading cause of concern in any medicated regimens. Pharmaceutical agents, when they surpass the therapeutic index, are the commonly identified causes for any illicit therapeutic effects or in some cases, even morbidity. Targeted therapy derives its roots from the concept of magic bullet, first elaborated and devised by Paul Erlich. Much later, as the understanding of cancer biology significantly progressed along with the mechanisms responsible for its initiation, promotion and progression, monoclonal antibodies developed. Various targets are involved here, which primarily consist of cell cycle proteins, hormones, growth factor receptors [1]. Nearly all drugs have potential for adverse drug reactions, hence there is always an imminent need to analyze the risk-benefit analysis and the overall ratio for prescribing the efficacious dose. The severity of these adverse drug reactions always vary as per age, gender, existing conditions, socio-economic differences, dosage regimens to name a few. These adverse drug reactions can be broadly classified into 3 different categories:

1. Idiosyncratic: These are generally not dose-related or allergic. They occur in a smaller proportion of patients.
2. Allergic: These are generally not dose-related and require some kind of previous exposure. After a patient is sensitized due to the drug acting as a primary allergen, further repeated exposure produces this allergic reaction.
3. Dose-related: This is a common occurrence for drugs with a very narrow therapeutic index.

### Symptoms

The underlying symptoms can generally be classified as mild, moderate, severe or extremely lethal. Sometimes, the drug symptoms are very difficult to be ascribed to one particular drug and may be the outcome of a subset of drugs. Some of the common symptoms include itching, rashes, difficulty in breathing, wheezing cough, asthmatic allergies and even hypotension [2].

### Psychedelic Drugs

Psychedelic drugs like Lysergic acid Diethylamide have potent uses of their own but are often plagued with severe side-effects at irregular dosing concentrations. Adverse reactions, generally classified as dysphoric or dysfunctional responses, require very careful clinical judicious use. There are always severe chances of organic brain damages with an irreparable damage towards personality, attitudes and the creativity loci in patients, who are undergoing regimens of these psychedelic drugs. They are supremely capable of producing forced states of altered perception, experienced generally in dreams. Lysergic acid Diethylamide-25 is often the regarded prototype for psychedelic compounds and is often the active ingredient in most of the other psychedelic compounds, sometimes labeled as mescaline or psilocybin. Overdoses of LSD can lead to death. The half-life of LSD is about 8 hours in humans and rapid tolerance is witnessed for these kinds of psychedelic drugs [3].

### Age-related Side Effects

Elderly people are prone to taking disproportionate amount of self-administered medications in certain cases. Elderly people over 65, consume about 30% of prescriptions and about 40% of over the counter products. Anti-depressants are widely used in elderly people, but they have to be prescribed with utmost care and caution, taking into consideration the concomitant drug history [4]. Tricyclic depressants (TCA) have been in use for over thirty years, and the gold standard against which current drugs are evaluated are imipramine and amitriptyline. However, authorities are cautioning elderly subjects to avoid these drugs due to their severe side-effects, which are off-setting the pharmacological effects [5-7].

### Anti-cholinergic Side Effects

Anti-cholinergic agents affect multiple systems causing a host of side-effects such as memory deficiencies, confusion, agitation, hallucination and delirium<sup>7</sup>. In patients with constipation, anticholinergic effects may lead to fecal impaction and also stomatitis. It is even alarming in patients with dementia as anti-cholinergic agents further inhibit cognitive performances and work against the pharmacological effects of cholinergic agents used to treat this disorder. In spite of these effects, anticholinergic agents are often prescribed for elderly patients, wherein more concerning cases of dementia and impaired cognition are witnessed [8].

### Side Effects Due to Non-Steroidal Anti-inflammatory Drugs (NSAIDs)

NSAIDs have been commonly used in the treatment of Osteoarthritis despite their increased risk of toxicity [2]. However, they have been limited because of the varied side effects such as erythema, dry skin and irritation. Gastrointestinal complaints and headaches are very commonly reported side effects, amongst the topical and oral NSAID categories [9]. Topical NSAIDs differ in terms of their formulation components (aqueous based or oil based), presence or absence of a permeation enhancer which improves the scope of permeation. Accordingly, these agents pose hurdles for site application toxicities. As per reports, vehicles such as Dimethyl Sulfoxide (DMSO) may be instrumental in contributing allergic and irritational side effects due to site application toxicities [10,11].

### Conclusion

In conclusion, toxicities due to pharmacological agents are an important factor to be considered while selecting a particular therapy, route and its dosage regimen. For the agent to exert its beneficial pharmacological effect, the therapeutic window of activity should be attributed foremost importance while screening parameters and any effect above this should aid in making an educated and informed decision regarding the toxic potential of these drugs.

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