

DRUG-INDUCED INJURY, ACCIDENTAL AND IATROGENIC

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Introduction

Drugs have been causing unintended injuries since time immemorial, but it is only in recent times that this phenomenon has attracted greater attention. An unprecedented proliferation of new and novel drugs and a greater legal awareness among the public have been two most important factors responsible for this change. Drug-induced injuries have been dubbed the cost of modern medical therapy. A few definitions may be discussed at the outset, if only for the purposes of recapitulation.

Drug

A drug may be defined as a single chemical substance or product that is used to prevent, diagnose, or treat disease or to alter the physiological state of the body. This definition includes substances, such as aspirin, which are ordinarily perceived as drugs, substances such as vaccines (used to prevent disease), radiocontrast agents (used to diagnose disease), and oral contraceptives (used to alter the physiological state of the body). Chemical substances such as heroin, cocaine, phencyclidine (PCP) and lysergic acid diethylamide (LSD) do alter the physiological state of the body, and in that sense, they can be construed as drugs. But for the purposes of this article, it would be more useful to conceive of them as “drugs of abuse,” rather than simply drugs. Their injurious effects will be dealt with in more detail elsewhere.

Medicine

A medicine is a mixture of one or more drugs with other ingredients which allow it to be delivered to the patient in a useful, stable, and palatable form. In addition to one or more drugs, a medicine includes stabilizers, sweeteners, and coloring matters. These excipients or pharmaceutical adjuvants can cause injuries in their own right.

Injury

Injury – in a legal sense, in most jurisdictions – is defined as any harm whatever done to a person in body, mind, reputation, and property. However, in a medical sense, injury can be defined as any harm done

to a person in body and mind. Injury in a medical sense is of more immediate concern for the purposes of this article.

Drug-Induced Injury

A drug-induced injury can be defined as an injury caused by a drug to a person. In rare cases, this injury can extend to, or even be limited to, some other person. Thus the sedative–hypnotic thalidomide caused no injury to pregnant mothers, but it caused phocomelia in their babies. Drug-induced injury can be intentional, as in parasuicide, but in this article, will only discuss accidental and iatrogenic drug-induced injuries.

Adverse Drug Reaction (ADR)

An ADR has been defined by the World Health Organization as an effect that is noxious and unintended, and that occurs at doses used in humans for prophylaxis, diagnosis, or therapy.

Medication Error

A medication error can be defined as an error in ordering, transcribing, dispensing, or administering a drug or medicine. A medication error may or may not cause injury.

Adverse Drug Event (ADE)

An ADE has been defined as an injury resulting from medical intervention related to a drug. This includes injuries related to a medication error and ADRs. The term “drug-induced injuries” roughly corresponds to “adverse drug events.”

Historical Overview

Drug-induced injuries have had medicolegal implications since the very dawn of recorded human history. As early as 2200 BC, the Code of Hammurabi stated that doctors should lose their hands if they caused the death of their patients. In the ninth century BC, Homer appears to have been aware of injuries caused by drugs. In *Odyssey* he mentions the fatal nature of drugs. Hippocrates, Galen, Rhazes, and Paracelsus were all aware of injurious effects of drugs. One of the earliest examples of a drug being officially banned due to severe adverse reactions was **antimony**, which was banned in 1566 by the Faculty of Medicine in Paris. William Withering (1741–1799), the discoverer

of digitalis, wrote about the injurious effects of digitalis as well. Recognizing the injurious effects of drugs, a preliminary kind of regulation on sales of drugs was passed in France in 1781.

The twentieth century witnessed some of the classical cases of drug-induced injuries, not the least important of which was the sulfanilamide–Massengill disaster of 1937, the Stalinon disaster of 1954, and the well-known thalidomide disaster of 1961. These three drug-induced disasters, occurring within a span of 25 years, took more than 200 lives and made more than 5000 people invalid. Sulfanilamide was a popular sulfa drug marketed in tablet and capsule form since the mid-1930s by the Massengill Company of the USA. During September–October 1937, the company decided to sell the drug in the form of an elixir too. Though an elixir could only be prepared in ethyl alcohol, the company decided to sell sulfanilamide in a solution of diethylene glycol without doing any preliminary testing in animals. Indeed, such testing was not legally required at that time. More than 100 people perished as a result of diethylene glycol poisoning. This disaster led to the passing of the Food, Drug and Cosmetic Act in the USA in 1938, and the Drugs and Cosmetics Act in India in 1940. Through these Acts, controls were exercised on the manufacture, sale, and distribution of drugs.

In 1954, the Stalinon disaster occurred in France. A French pharmacist invented Stalinon for boils. The medication contained 15 mg diiodoethyltin and 100 mg isolinoleic acid esters. Tin is toxic to the human central nervous system. Several people showed signs of raised intracranial pressure, such as headache, confusion, and vomiting. About 102 people died and about 100 more were permanently affected. Some survivors had residual paraplegia. It was discovered that clinical trials had been done, but with capsules containing just 3 mg diiodoethyltin – instead of the supposed 50 mg – due to a dispensing error. The patients thus received five times the drug that had been tested in clinical trials. In 1957, the pharmacist was sentenced to two years imprisonment and heavily fined.

The biggest of all drug-induced disasters was undoubtedly the thalidomide disaster, occurring in the late 1950s and early 1960s. During this period, this drug was marketed in more than 40 countries – mainly in West Germany, the UK, and Japan. In Germany, it was manufactured by Chemie Grünenthal and marketed by it as Contergan from 1956, and enjoyed good sales. In the UK it was licenced by Chemie Grünenthal to the Distillers Company. It was available in the UK from the beginning of 1958 as Distaval. In Sweden, the license was given to a local company, Astra. The drug could not enter the USA,

thanks to the Food, Drug and Cosmetic Act, 1938, which had been passed because of the earlier sulfanilamide–Massengill disaster. It was being used by pregnant women to counteract nausea, which is usually seen in early pregnancy. It also acted as a sedative, and was touted as the safest sedative–hypnotic in the field. Yet it proved to be a strong teratogen, causing limb deformities in newborns known as amelia (absence of limbs) and phocomelia (seal limbs). Women who took it between the fourth and eighth week of pregnancy suffered most, as limb buds start to form during this period. An estimated 5000–10 000 deformed children were born around the world due to this drug. It was finally taken off the shelf in 1961. Nevertheless it was responsible for the amendment of the Drugs and Cosmetics Act, 1940 of India (in 1964), and the passing of the Medicines Act in the UK (in 1968). It is an unfortunate fact that it has taken some of the worst drug-induced disasters of history for the governments around the world to pass acts related to safe use of drugs.

Table 1 gives some recent examples of drugs being withdrawn because of drug-induced injury, or that resulted in heavy compensation claims.

Therapeutic Index

The dose of a drug required to produce a specified beneficial effect in 50% of the population is called the “median effective dose,” and this is abbreviated as ED₅₀. The median lethal dose of a drug – as determined in experimental animals – is the dose that would kill 50% of the population. It is abbreviated as LD₅₀. Clearly the relationship between LD₅₀ and ED₅₀ would determine the safety of any given drug. The higher the ratio, the safer the drug. Mathematically speaking: Therapeutic index of a drug = LD₅₀/ED₅₀.

Figures 1 and 2 clarify the concept. **Figure 1** shows the dose–response curve of a very safe drug. On the *x*-axis is represented the logarithm of the drug dose and on the *y*-axis, the percentage of people showing a given effect – beneficial or lethal. Fifty percent of the population shows a beneficial effect with 100 mg of the drug. LD₁ of the drug – the dose at which just 1% of the population will show fatal results – is around 450 mg, which is far greater than 250 mg, at which 99% of the population shows the beneficial effect (ED₉₉). This is a very safe drug, having a very high therapeutic index (8.0). There is practically no chance of fatality occurring with this drug.

Figure 2 shows the dose–response curve of an unsafe drug. The two curves – those for the beneficial effect and lethal effect – are very closely spaced. Its ED₅₀ is 200 mg, while LD₅₀ is 400 mg. The therapeutic index is just 2.0.

Table 1 Recent cases of drugs being withdrawn because of drug-induced injury, and/or resulting in heavy compensation claims

<i>Drug</i>	<i>Chemical name</i>	<i>Company</i>	<i>Indicated for</i>	<i>Mode of action</i>	<i>Why withdrawn</i>	<i>Date withdrawn</i>
Alosetron hydrochloride	lotronex	Glaxo Wellcome	Diarrhea-predominant irritable bowel syndrome (IBS) in women only. Not found effective in male patients	Controversial. Could be its highly selective antagonism of 5HT ₃ -receptors	Ischemic colitis, severe constipation leading to intestinal obstruction and ruptured bowels. Some of the patients who survived required surgical removal of sections of their intestines	November 28, 2000 (approved on February 9, 2000)
Baycol	cerivastatin	Bayer Pharmaceutical Division	Lowering cholesterol	Belongs to a class of drugs known as statins. These drugs are competitive inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, which catalyzes an early rate-limiting step in cholesterol biosynthesis	Reported to cause myopathy or rhabdomyolysis which can lead to kidney damage and death from acute renal (kidney) failure	August 8, 2001
Celebrex	celecoxib	Pharmacia	Rheumatoid arthritis, osteoarthritis, reducing the number of intestinal polyps in patients with a rare genetic disorder called familial adenomatous polyposis (FAP)	Selective inhibitor of cyclooxygenase-2 (COX-2), thereby inhibiting the synthesis of prostaglandins and thromboxane. Drugs that inhibit both COX-1 and COX-2 (such as aspirin) cause more side-effects such as gastric ulcer (due to inhibition of COX-1)	Increased the risk of heart attack and stroke	A "warning letter" was sent on February 1, 2001, by US FDA to Pharmacia
Fen/Phen	fenfluramine + phentermine	American Home Products	Weight reduction	Same as that of redux	Same as that of redux	Not yet recalled
Pondimin	fenfluramine	American Home Products	Weight reduction	Same as that of redux	Same as that of redux	September 1997
PPA	phenylpropanolamine	Several	An active ingredient of medications for nasal decongestion and weight reduction	Sympathomimetic amine	Increases the risk of hemorrhagic stroke in women. Men may also be at risk	2000
Raxar	grepafloxacin	Glaxo Wellcome	An antibiotic used to treat bacterial infections such as bronchitis, community-acquired pneumonia, gonorrhea, urethritis, and cervicitis	Similar to those of quinolones	Prolongation of the QT interval resulting in ventricular arrhythmias in some patients	October 1999

Redux	dexfenfluramine (dextro-isomer of fenfluramine)	American Home Products	Weight reduction	Controversial. Sympathomimetic amine. Promotes rapid release of serotonin and inhibits its reuptake, thus causing profound changes in its levels in the brain	Heart valve damage, primary pulmonary hypertension	September 1997
Rezulin	troglitazone (belongs to a class of drugs known as thiazolidinediones)	Warner-Lambert	Diabetes	Selective agonist for nuclear peroxisome proliferator-activated receptor-gamma (PPAR)	Severe hepatic toxicity	March 2000 (had been marketed since March 1997)
Serzone	nefazodone HCl	Bristol-Myers Squibb	Antidepressant	Atypical antidepressant	Severe hepatic toxicity. Concomitant use of Serzone and Zocor can cause rhabdomyolysis	January 2003 (from the European market) because of its link to 25 reports of liver failure and 18 deaths. November 2003, from Canada. A "black-box" warning on the labels is necessary in other places. (Had been approved by the FDA in 1994)
Vioxx	rofecoxib	Merck	Osteoarthritis, menstrual pain, management of acute pain in adults	Same as that of Celebrex	Same reasons as those for Celebrex	A "warning letter" was sent on September 17, 2001, by US FDA to Merck
Xenadrine	ephedra	Cytodyne Technologies	Weight reduction	Controversial	Associated with a number of side-effects: high blood pressure, irregular heartbeat and heart palpitations, insomnia, nervousness, dizziness, gastrointestinal distress, hepatitis, psychosis, tremors, headaches, seizures, heart attack, stroke, death	Not yet withdrawn, but a number of compensation claims have been made against the manufacturing company

FDA, Food and Drug Administration.

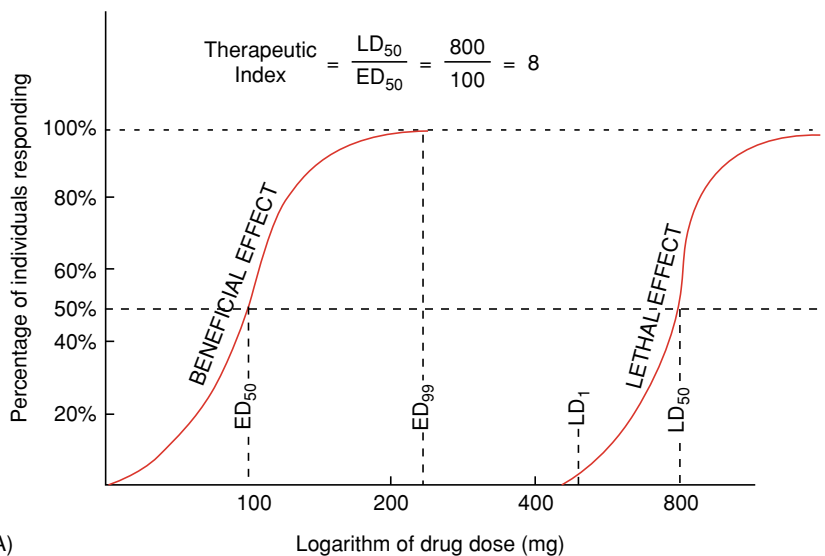


Figure 1 Dose–response curve of a safe drug.

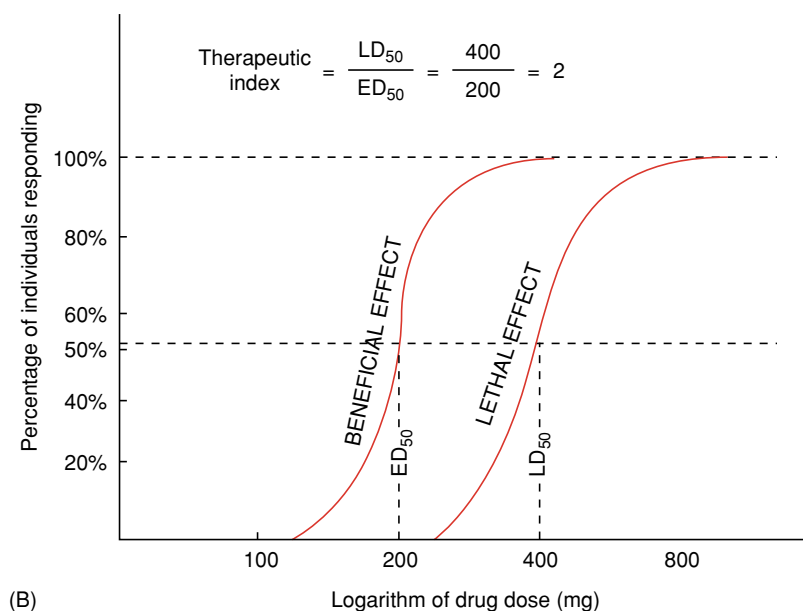


Figure 2 Dose–response curve of an unsafe drug.

Adverse Drug Reactions

ADRs have been grouped into two main categories – type A or augmented reactions and type B or bizarre reactions. Type A ADRs are simply the exaggerated manifestations of the drug’s very own pharmacological actions. Typical examples include hypoglycemia occurring with insulin, bradycardia with beta-adrenoceptor antagonists, suppression of bone marrow with anticancer drugs, hemorrhage with anticoagulants, loss of coordination with

anticonvulsants, drowsiness with benzodiazepine anxiolytics, and unstable heart rhythms with digoxin. Type A reactions are largely predictable on the basis of the drug’s known pharmacology. Their incidence and morbidity in the community are quite high, but their mortality is generally low. Generally, type A reactions are more likely and more serious for drugs that have a low therapeutic index.

Type B ADRs are totally aberrant effects that cannot be predicted; nor do they bear any semblance to the drug’s normal pharmacological actions.

Malignant hyperthermia of anesthesia and allergic reactions to penicillin, iodine-containing radiopaque dyes used in radiology, and various vaccines and sera fall into this category. Their incidence and morbidity in the community are usually low, but their mortality may be quite high. Since their incidence in the community is low, they are not usually observed during conventional toxicological screening programs.

Some commentators have added three more categories. These are: (1) type C or chronic treatment reactions; (2) type D or delayed reactions; and (3) type E or end-of-treatment adverse effects. Type C reactions only become apparent after very long treatment. Typical examples are iatrogenic Cushing's syndrome, produced after months of treatment with corticosteroid drugs, and orofacial dyskinesia following long treatment with chlorpromazine.

Type D, or delayed-type ADRs, are seen many months or years after the treatment has ceased. They can even be seen in future generations – those that did not ingest the drug at all. The classical example here of course is teratogenicity induced by thalidomide and other teratogenic agents, and stilboestrol producing clear-cell carcinoma of the vagina in the daughters of mothers treated with it in pregnancy. Another good example is the appearance of fetal calvarial hypoplasia and kidney failure in newborns after their mothers have been exposed to angiotensin-converting enzyme (ACE) inhibitors such as lisinopril, captopril, and enalapril.

Type E or end-of-treatment adverse effects appear at or after the end of treatment, and mostly represent “rebound phenomena.” Examples are rebound anxiety and insomnia after cessation of treatment with benzodiazepines, rebound hypertension after cessation of treatment with clonidine, and unstable angina appearing after abrupt withdrawal of beta-blockers.

Medication Errors

Medication errors are frequent causes of legal actions being brought against pharmacists, nurses, and doctors. Fortunately they are completely avoidable. A quick look into how medication errors occur will help the healthcare provider avoid them.

Failed Communication

Communication errors between the prescribing physician and the dispensing chemist can occur because of a number of reasons. Poor handwriting, drugs dictated over the telephone, drugs with similar names, a confusion with zeros and decimal points, a confusion of metric and apothecary systems, and ambiguous abbreviations can all cause failed communication,

leading to a medication error. Look-alike names such as Losec (omeprazol, a gastrointestinal drug) and Lasix (furosemide (frusemide), a diuretic) – combined with poor handwriting – can lead to a medication error, as can sound-alike names such as Taxol (paclitaxel, an anticancer agent) and Paxil (paroxetine, an antidepressant) spoken over the phone. In addition, it is quite possible for a patient to hear “two tablespoonsful,” when what the physician actually said was “two teaspoonsful.” For these reasons, as far as possible, the physician should avoid prescribing over the phone. The only situation where a physician can perhaps be excused for prescribing over the phone is when an emergency situation has arisen, and the physician thinks that he/she can probably save a life by prescribing over the phone.

Confirmation Bias

Paradoxically, an experienced pharmacist is more likely to fall prey to this than a newcomer. Confirmation bias refers to a person's tendency to extrapolate what he/she has seen, without actually seeing.

Figure 3 presents an example of confirmation bias. Familiarity with the name of a book can make many readers extrapolate what they have seen, and be blind to an inherent mistake. The figure here shows a repetition of “of.” A chemist who has been dispensing heparin frequently (and is thus familiar with its name), would tend to read a prescription of Hespan (hetastarch, sodium chloride) as heparin. Cases have occurred where nurses have infused heparin when they should have infused Hespan.

Dose Miscalculations

Doses usually have to be calculated according to the weight of the patient; this is particularly true of pediatric patients. A simple mistake in division can cause a 10-fold mistake in dosages. Studies have shown that 10-fold mistakes in dosage calculations can occur as frequently as 15% of the time.

Incorrect Drug Administration

Cases have occurred where a medicine meant for one patient has been given to another patient. This mistake can occur when two patients in the same ward had the same name or similar-sounding names and the dispensing nurse was careless. Drugs may be given through a wrong route. BAL meant for deep intramuscular injection, if given by the intravenous route

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Figure 3 What is wrong here? Example of confirmation bias.

can cause serious fat embolism (it comes dissolved in arachis oil). Drugs meant for the oral route (enteral feeding supplements), or irrigations meant for the bladder, given through the intravenous route can cause disaster. Instances of topical medications being swallowed and ear medications being instilled in the eye (and vice versa) are well known.

Poor Drug Distribution Practices

Poor drug distribution practices that have resulted in medication errors include keeping a dangerous product next to one which looks just like it (causing drug mix-ups), relying too much on computer-generated labels, and automated dispensing equipment (if wrong information was inadvertently fed into the computer, it can lead to serious errors), and untrained persons gaining access to the pharmacy. Night-duty nurses are known to enter the pharmacy after regular hours (when the regular pharmacist has left), and pick up drugs on their own.

Nearly Identical Labeling

Two separate items are sometimes labeled with quite similar-looking labels. This can cause a dispensing error. There was a time when the packaging for the antibiotic metronidazole was quite similar to that of mivacurium, a neuromuscular blocking agent. This caused several mix-ups. The labeling has now been revised. Extemporaneously prepared labeling produced by in-house pharmacists can sometimes cause unintentional mix-ups.

Lack of Patient Education

Studies have shown that if a patient is properly educated about a medication, e.g., what it looks like, its correct route of administration, permissible alternative routes of administration, correct dosage, when it should or should not be taken, there are fewer chances of an incorrect administration of drug. Thus health professionals should spend more time with their patients, explaining about the medication. Patients should be encouraged to ask questions.

Medicolegal Aspects

In recent years, there has been an unprecedented growth in medical litigation, especially in relation to drug-induced injuries. In these cases, it is usual for the defendant to challenge the causation – the fact that the drug was responsible for the injury alleged. In a case as straightforward as that of thalidomide, all the nine senior members of Chemie Grünenthal (who were tried in a criminal court in Aachen) disputed the causation, and experiments had to be conducted in rabbits to demonstrate a similar teratogenic effect

(despite this, the criminal trial was abandoned after two years, and the civil case was decided out of court for 114 million Deutschmarks).

Causation

In determining the real link between the drug and the injury (the causation) the court usually has recourse to a few standard pointers:

1. The patient must have been exposed to the drug.
2. The exposure must have occurred before the alleged injury.
3. The time period between the exposure and injury should be sufficient.
4. The extent of exposure must account for the alleged injury (i.e., a sufficient quantity of drug was given for a sufficient time).
5. Where the injury is temporary it must disappear with the cessation of drug and reappear with the start of reexposure (a strong pointer).
6. The alleged injury must be a known complication of the drug, if the drug is already in use.
7. The injury can best be explained in terms of exposure to the drug, and not by any other concomitant factor.
8. In the case of new and novel drugs, experimentation in animal models must produce a similar injury.

The physician must show that he/she had taken “reasonable care” when prescribing the drug. This means that an average physician of his/her rank, specialty, experience, expertise, and seniority would have done the same. A recent case that illustrates this legal principle aptly is *Cranley v. The Medical Board of Western Australia* [1992] Med LR 94. In this case a physician, Cranley, prescribed drugs like diazepam, dextropropoxyphene, and flunitrazepam to drug addicts for self-administration, including by injection. This was not normal “mainstream practice” as defined in the Australian National Methadone Guidelines, which envisaged the substitution of only oral methadone for intravenous heroin. However, the Supreme Court of Western Australia held Cranley not guilty (of a charge of misconduct) and found that there was a reputable minority approving of the policy adopted by Cranley. It also accepted the evidence of Dr. Pols, a leading expert in the treatment of addiction, who gave evidence that in appropriate circumstances, parenteral diazepam for self-administration could be prescribed.

The following cases do not pretend to give a comprehensive coverage of drug-related litigation, but serve as useful pointers to various facts courts take into consideration when pronouncing a health-care provider liable or not liable.

Decisions Against the Healthcare Providers

In *Murray v. Thrifty Drug Store*, Cal. Super. Ct., Sacramento Co., docket no. 209949, 1972, a 70-year-old woman, a sufferer of arteriosclerotic heart disease with chronic atrial fibrillation, congestive heart failure, anginal syndrome, and uncontrolled diabetes mellitus was wrongly given gout medication by the pharmacist. She suffered a heart attack subsequently and claimed that the wrong medication was responsible for it. Although a claim for \$75 000 was made, the jury awarded her \$3000.

In *Snell v. Curtis*, Mich. Cir. Ct., Wayne Co., docket no. 119586, 1971, a physician gave methotrexate to his patient continuously for 43 months as a treatment for psoriasis. Chronic administration of methotrexate is known to cause hepatic fibrosis and cirrhosis, which can be detected in its early stages by regularly conducting liver function tests. The physician however not only failed to conduct these tests, but continued to administer the drug even after spider angiomas developed (a sign of hepatic cirrhosis). The treatment was continued for 11 months after the angiomas first appeared. Finally the patient was admitted to a hospital where a diagnosis of cirrhosis of the liver was made. The patient died after five months. The court awarded \$200 000 to the patient's estate.

Decisions in Favor of Healthcare Providers

In one case (US Dist. Ct. District of Columbia, no. 1356-58, August 1963), a four-year-old girl died of aplastic anemia after she was prescribed chloramphenicol by a doctor. Aplastic anemia is a known complication of chloramphenicol, but it occurs only in one case out of approximately 800 000. The court maintained that negligence cannot be inferred simply from the fact that treatment was unfavorable. It was the family's responsibility to prove that the doctor was unskillful or negligent, and they had failed to prove that. A rare complication of a drug is not sufficient to prove the doctor's negligence. The father of the deceased child also argued that the pharmaceutical firm manufacturing the drug had failed to warn. To this, the judge said that chloramphenicol was a prescription drug and could only be obtained on a doctor's prescription. Thus the manufacturer had no duty to warn the public directly (the learned intermediary principle).

In *Mickles v. State of New York*, 252 N.Y.S. 2d 629, the plaintiff, who had been suffering from *Shigella flexneri* dysentery, was prescribed tetracycline (Tetrex), following which she had a reaction with high fever. In its judgment, the court held that there was evidence that this was a routine treatment in such

cases and if a qualified doctor stays within approved methods, he/she is not required to anticipate results from a patient's peculiar characteristics.

Drugs Prescribed via Telephone

If the physician has to prescribe via telephone, he/she must maintain a proper telephone message form detailing the name, age, sex, address, and telephone number of the patient, the date and time of call, the symptoms the patient described, and the drug, dosage, and route the physician advised. This form should be properly filed in the patient's folder if he/she is a current patient. In the case of new patients, a new patient folder must be created, and the form kept there. All telephone prescriptions must be confirmed with the pharmacist as far as possible. If the patient does not contact the physician again, it would be a good idea for the doctor to make an unsolicited call to the patient and confirm the medications the patient has been taking, and if he/she has been experiencing any new symptoms. These simple measures can go far in preventing any uncalled-for litigation.

The following case (citation 25: 147, Sept 1, 1972, published by American Medical Association) aptly illustrates the hazards of prescribing over the telephone. In 1962, a patient saw a physician for a skin rash for which he was prescribed triamcinolone (Aristocort) to be taken orally. It was apparently effective. From that point onwards, whenever the patient had the rash, he was always prescribed the same drug. This went on for four years. In 1966, the patient went to another clinic where he was seen by another physician (physician 2), who also prescribed the same medication. Thereafter the second physician would always prescribe Aristocort over the phone, without bothering to make a physical examination. In 1967, the patient visited the clinic again, where he was examined by a third physician (physician 3), who found that the patient had developed Cushing's syndrome, and stopped the medication. The patient sued physician 2, because he had been prescribing him over the phone without caring to make a physical examination. The jury agreed and awarded him \$460 358 in damages.

Vaccine-Induced Damages

Vaccines have been known to cause injuries, and one of the best examples is that of pertussis vaccine causing irreversible brain damage in children. Several court cases have been fought over this issue. (According to one estimate, in 1985 in the USA an estimated 11 lawsuits were filed for every million doses of vaccine distributed. The vaccine manufacturers spent \$16.2 million in settling 52 of them out of court.) In

many cases the court found that the doctor was not guilty. One of the most publicized of these was the so-called Susan Loveday case (*Loveday v. Renton and the Wellcome Foundation* [1990] 1 Med LR 117). In this case Susan Loveday, a young child, suffered irreversible brain damage after being administered pertussis vaccine by a general practitioner. Boroughs Wellcome – the manufacturers of the vaccine – were never sued in the first place, but they became co-defendants at their own request. Lord Justice Stuart-Smith in his 300-page judgment held that the general practitioner and the manufacturing company were not liable.

In all cases where a vaccine has to be administered, the doctor would do well to obtain written informed consent from the parents, whereby all risks and benefits are explained to them.

Packaging and Storage of Medicines

The use of outdated medicines can result in adverse reactions. Manufacturers must ensure that the date of expiry is prominently displayed on all medications supplied by them. The medicine must remain safe during this period. An outbreak of Fanconi's syndrome has been linked to the use of old tetracycline, which had become chemically degraded.

Drug Automatism

Some drug-induced deaths, especially those involving barbiturates, have been explained away as being due to a rather mythical phenomenon called “drug automatism.” This means that a patient – in a kind of automatic behavior – repeatedly took the drug, poisoning him/herself to death. This has been stated to be due to confusional states. Another explanation is that the patient forgot that he/she had taken a pill, before taking another, and the cycle went on until the patient poisoned him/herself to death (according to this explanation, the ingested drug itself was responsible for the patient's amnesia). These arguments were undoubtedly raised to beat the “no-benefit-in-case-of-suicide” clause inherent in most life insurance policies. With our current knowledge of therapeutic, toxic, and lethal blood levels of drugs, such an argument is unacceptable today. For instance, even if a patient started taking, say, barbiturates in a confusional, somnolent, or amnesic state, he/she would fall unconscious well before blood levels reached fatal levels.

Prevention of Drug-Induced Injuries

Drug-induced injuries may be almost unavoidable in the modern setting. We may wonder what we would do if given the choice of risking a deadly disease versus swallowing a risky pill to counteract it. Nevertheless, if we do not want the risk of a disease, we have to take the risk of the drug! What we must ensure however is that the risk–benefit ratio of any given drug is in the patient's favor. This can be ensured by tight drug monitoring and control systems and a stringent toxicovigilance program.

See Also

Complaints Against Doctors, Healthcare Workers and Institutions; Drugs, Prescribed: Product Liability; **Medical Malpractice – Medico-legal Perspectives:** Negligence Quantum; **Pharmacology of Legal and Illicit Drugs; Substance Misuse:** Miscellaneous Drugs

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