Review Article

Drug Tragedies to Drug Safety: A Comprehensive Review of ADR-Driven Regulatory Reforms

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ABSTRACT

The evolution of current pharmacovigilance procedures and drug regulatory frameworks worldwide has been significantly impacted by past drug tragedies. Significant flaws in drug safety assessment and monitoring processes were revealed by tragic incidents involving medications like thalidomide, sulfanilamide, and diethylstilbestrol. Serious adverse drug reactions (ADRs), such as birth defects, toxic consequences, and long-term health issues, were the outcome of these instances. This analysis examines these significant pharmaceutical disasters and assesses how they have influenced the development of pharmacovigilance and drug safety laws. It describes how these incidents prompted the implementation of more stringent preclinical and clinical procedures for medication approval. The study also emphasises the significance of ongoing safety monitoring, efficient risk assessment, and evidence-based prescription procedures, particularly for high-risk populations like expectant mothers.

Keywords: Pharmacovigilance, Safety monitoring, Adverse Drug Reactions (ADRs), Birth defects, Thalidomide, Sulfanilamide, Diethylstilbestrol, Risk assessment.

INTRODUCTION

OVERVIEW OF PHARMACOVIGILANCE:

Following the publishing of a letter by William McBride in The Lancet, the World Health Organization officially acknowledged the idea of pharmacovigilance (PV) in December 1961. In this article, he proposed a potential link between Thalidomide use during pregnancy and severe congenital malformations, including phocomelia. Pregnant women were frequently prescribed thalidomide at the time as a sedative and antiemetic drug to treat morning sickness. The WHO launched the "Program for International Drug Monitoring" in 1968 to improve drug safety monitoring worldwide.

In order to discover prospective pharmacovigilance signals as soon as feasible, this project was created to gather and centralise reports of adverse drug reactions (ADRs) from all over the world. Later, in the middle of the 1970s, a group of French toxicologists and pharmacologists used the phrase "potential visceral" to refer to tasks including the assessment and tracking of risks connected to side effects of medication therapy.[1]

The scientific field that deals with the identification, gathering, tracking, evaluation, and assessment of side effects associated with medications and medical supplies is known as pharmacovigilance. It entails asking patients and medical professionals about the safety of medications, vaccines, biological products, blood products, herbal remedies, medical equipment, and complementary or alternative therapies. Pharmacovigilance's main goals are to avoid medication-related injury and to identify potential dangers related to these goods.

THE HISTORICAL CONTEXT OF PHARMACOVIGILANCE:

Drug safety was not a significant worry for either patients or medical personnel in the early years of medication use. But the 1960s Thalidomide catastrophe was a watershed moment that made regulators and medical professionals realise how crucial medication safety is. The United States Food and Drug Administration Act was first passed in 1906, but significant changes were made after the use of diethylene glycol as a solvent in sulphanilamide elixir resulted in 107 fatalities. This terrible event brought to light the risks associated with insufficient medication regulation and resulted in more stringent regulation of pharmaceutical ingredient misbranding and misleading therapeutic claims. The international thalidomide tragedy, which was initially documented in December 1961, further changed drug safety laws around the globe. Prior to this catastrophe, safety evaluation was given relatively less consideration than the effectiveness of medications, which was thought to be the main criterion for drug approval. After the event, more focus was put on making sure medications were safe and effective before they could be sold. Because of this, the USFDA Act was changed in 1962 to require new medications to provide safety and efficacy data prior to marketing. The "Yellow Card System" for tracking adverse drug responses was first developed in 1964 to enhance post-marketing surveillance, and the Medicines Act was put into effect in the UK in 1968. Following the creation of the World Health Organization Programme for worldwide Drug Monitoring (IDM) in 1968, which bolstered worldwide pharmacovigilance efforts, drug safety monitoring became more structured and globally coordinated.[1]

PHARMACOVIGILANCE SIGNIFICANCE IN HEALTHCARE:

In order to ensure the safe use of medications and other medical interventions and to improve patient care, the contemporary pharmacovigilance system is crucial. Its main goal is to safeguard public health by lowering the dangers of drug therapy and encouraging community members to utilise medications safely. The ongoing assessment of the advantages, dangers, efficacy, and potential negative effects of medications is also supported by pharmacovigilance. This continuous observation aids medical practitioners in promoting the sensible, suitable, and economical use of medication therapy. Additionally, the system encourages healthcare personnel to have more clinical training, education, and awareness regarding pharmacovigilance. The efficient dissemination of medication safety information to the general population is another crucial aspect of pharmacovigilance. It helps prevent misuse and lowers the incidence of negative drug-related consequences by raising awareness about the appropriate use and possible hazards of medications.

The World Health Organization's pharmacovigilance program has continued to change over time in response to the shifting healthcare requirements and capabilities of its member nations. In order to promote worldwide pharmacovigilance procedures and global drug safety standards, nations are highly encouraged to actively participate and collaborate, since they provide innovation, improvement, and useful insights.[1]

THE IDEA OF AN ADVERSE DRUG REACTION:

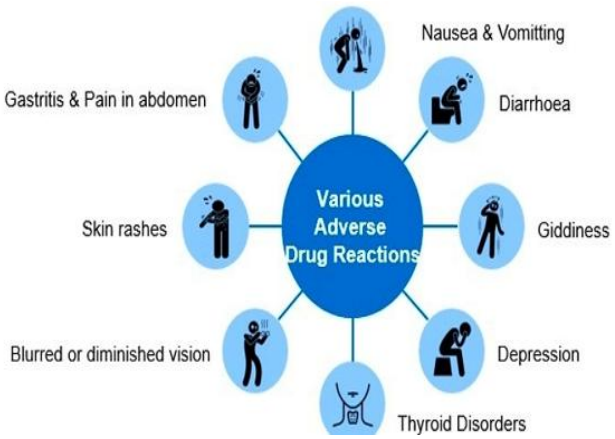

Figure 1: Different Adverse Drug Reactions

An adverse drug reaction (ADR) is described by the World Health Organization as a negative and unexpected reaction to a medication that happens when the medication is given at recommended dosages for the prevention, diagnosis, or treatment of illness, or for altering physiological processes.[2] For many years, this definition has been frequently utilised in pharmacovigilance practice.

Different kinds of adverse drug reactions:

Based on their pattern, cause, and clinical presentation, adverse drug reactions (ADRs) are divided into various categories:

Type A: (Augmented) reactions occurs because of a drug's recognised pharmacological activity, that are predicted. These reactions are typically common, dose-dependent, and simpler to recognise. Hypoglycemia brought on by insulin injection is a common case.

Type B: (Bizarre) reactions are rare, erratic, and typically unrelated to the typical dosage of the medication. They frequently happen abruptly, are severe, and are uncommon. One well-known instance of this kind of reaction is penicillin-induced anaphylaxis.[3]

Type C: (Chronic) responses can occur after taking drugs for an extended period of time. With ongoing medication exposure, these effects are frequently detectable and predictable. Analgesic nephropathy linked to prolonged analgesic usage and benzodiazepine dependency are two examples.[3]

Type D: (Delayed) reactions occurs due to long-term exposure to medication. One example of this group is thought to be carcinogenesis.

Type E: (End-of-use) reactions take place when long-term treatment is abruptly interrupted. While stopping opioids can cause withdrawal symptoms, stopping corticosteroids abruptly can cause rebound adrenocortical insufficiency.[3]

Type F: (Failure of therapy) reactions take place when a medication does not have the desired therapeutic effect. For example, bacterial resistance may make antibiotics ineffective, leading to treatment failure.

PHARMACOVIGILANCE'S FUNCTION IN ADR MONITORING:

In reaction to events that highlighted the significance of safe and responsible drug use, a number of laws and regulations have been created over the years. The US Food and Drug Administration's post-marketing surveillance mechanism came under heavy fire after Sulfanilamide was taken off the market. As a result, better pharmacovigilance systems were created with the goal of more successfully recognising, tracking, and disseminating drug-related dangers. Adverse drug reaction (ADR) monitoring is the continuous practice of identifying and tracking negative or unexpected effects linked to medications. In this sense, pharmacovigilance is essential for detecting, evaluating, and averting adverse drug responses, which enhances patient safety and encourages the safer use of medications.[4]

GOAL OF THE REVIEW:

By analysing notable pharmaceutical tragedies that have had a substantial impact on public health worldwide, this analysis focuses on the historical development of medication safety. It seeks to investigate how these terrible events prompted the creation and application of more stringent safety regulations. Understanding how these restrictions enhanced safety monitoring protocols, drug approval systems, and general medicine regulation practices is given special attention. The evaluation also assesses how well these legislative and regulatory actions work to lessen the possibility that tragedies of this nature

would recur. It also emphasises the ongoing necessity of bolstering pharmacovigilance systems to guarantee safer treatment results and improved global public health protection. In order to guarantee the safe and efficient use of medications, the study highlights the significance of thorough preclinical and clinical research, adherence to stringent ethical standards, and ongoing post-marketing surveillance.

DRUG RELATED TRAGEDIES:

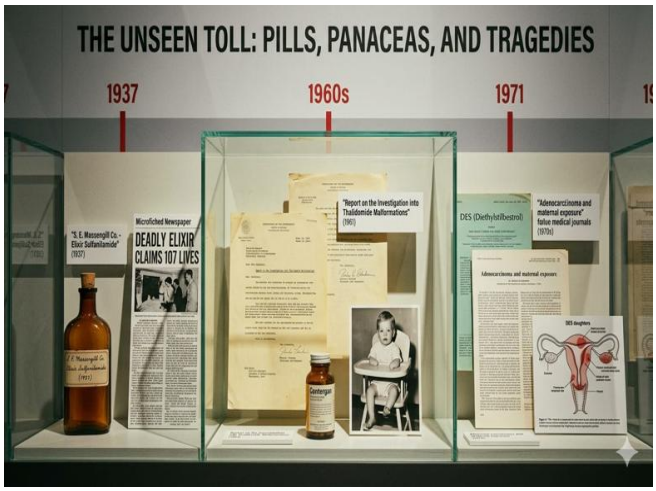

Figure 2: Tragedies, Pills, and Panaceas: The Unseen Cost

Drug tragedies are instances where pharmaceutical products result in extreme adverse reactions, widespread injury, or patient death. These catastrophes can be caused by unanticipated hazardous effects, manufacturing mistakes, or unethical medical and pharmaceutical procedures. They frequently result in congenital anomalies, lasting impairments, or a substantial loss of human life. A new medication must pass rigorous preclinical and clinical testing to guarantee its safety, efficacy, and acceptable quality before it is authorised for general use. Regulatory bodies in various nations carefully examine the data produced by these investigations. In India, the Central Drugs Standard Control Organization oversees these evaluations. The New Drug Application (NDA) and the Investigational New Drug (IND) application are two significant regulatory filings that are part of the approval process. The IND application is filed to offer continuing safety information throughout the research process and to get permission to conduct clinical trials. To get permission to sell and commercialise a novel medication, an NDA is filed. Manufacturers file an Abbreviated New Drug Application (ANDA), which is expressly meant for generic drug approval, in the case of generic medications. Post-marketing surveillance, in which patients using the medications are closely watched for side effects, keeps an eye on the safety of pharmaceuticals even after they are put on the market. The goal of preclinical research, clinical trials, regulatory applications, and ongoing communication with regulatory bodies is to maintain the safety and efficacy of pharmaceuticals for patient use. Serious adverse medication responses, long-term harm, or even death may occur if these requirements are not upheld. Numerous pharmacological catastrophes have occurred throughout history, with catastrophic results that have killed countless people and permanently damaged many more.[5]

DRUG TRAGEDIES IN HISTORY:

Several significant case studies of prior drug tragedies that led to grave health risks and perhaps fatal circumstances are shown here. Global healthcare standards, pharmacovigilance procedures, and drug safety laws have all improved significantly as a result of these instances.

A.THE THALIDOMIDE TRAGEDY (1961):

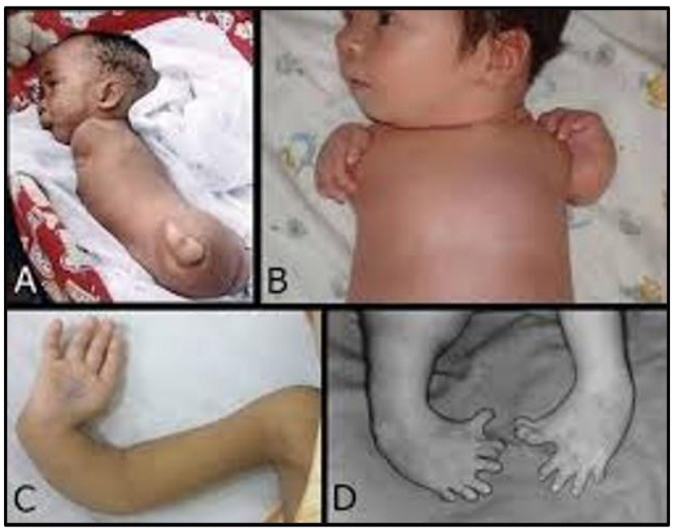

Figure 3: Newborn Limb Abnormalities

1. Introduction of Drug:

Chemie Grünenthal, a German pharmaceutical company, introduced thalidomide as a sedative in the late 1950s, promoting it as safer and less addictive than barbiturates. The medication quickly became well-known due to its efficacy, especially in treating nausea and vomiting. It was frequently administered to expectant mothers to treat morning sickness because of its antiemetic qualities. Thalidomide was sold under many trade names in almost 46 countries as its use grew. It was marketed as Distaval in the UK and Australia and as Softenon in a number of European nations.[6]

2. Background:

When thalidomide was first launched, drug testing protocols were far laxer than they are now, and adequate testing for teratogenic or birth defect-causing effects was not carried out. This inadequate safety review led to the drug's quick approval and widespread distribution in many nations. Due to its successful antiemetic action in pregnant women suffering from morning sickness, thalidomide quickly gained widespread popularity. Its affordable price and easy accessibility without a prescription further promoted its widespread use. With almost 14.6 of tonnes sold in 1960 alone, the medication swiftly became one of the most popular sedatives in Germany.[7]

3. Pharmacology of Drug:

Chemically speaking, thalidomide is categorised as a racemic derivative of glutamic acid, with equal proportions of the R-(+) and S-(–) enantiomers. These two forms can quickly interconvert under normal physiological settings in the body, making it challenging to distinguish and investigate their distinct biological impacts in live systems. According to research, the R-enantiomer is more closely associated with the drug's sedative effects, whereas the S-enantiomer is primarily important for preventing mononuclear blood cells from releasing tumour necrosis factor-alpha (TNF-α). Furthermore, under physiological conditions, the thalidomide molecule might spontaneously hydrolyse due to its chemical instability.[7]

4. Occurrence of Adverse Drug reaction:

Thalidomide was sold under various brand names in almost 46 countries worldwide. When doctors started giving them free trial packets, particularly to pregnant patients experiencing morning sickness, its use grew even more. The precise number of women who were exposed to the drug during this time, however, has never been established. Reports of side effects began to surface shortly after thalidomide became popular. Peripheral neuropathy was a common side effect of the medication. Newborns with the severe congenital defects affecting several organ systems were being reported at the same time. At first, these birth abnormalities were either purposefully ignored and disregarded or were not linked to thalidomide use. Thalidomide exposure during pregnancy was clearly linked to severe foetal deformities in 1961, according to two independent specialists, William McBride in Australia and Widukind Lenz in Germany. More than 10,000 children were born with severe birth deformities as a result of one of the most catastrophic man-made medical catastrophes in history, according to their findings.[6]

5. Nature of Tragedy:

Due to serious congenital anomalies affecting the limbs, a five-month-old male newborn was placed under medical observation. Deafness, phocomelia, anomalies of the gastrointestinal tract, facial and palate deformities, and the lack of arms and ears were among the documented foetal malformations. Subsequent research revealed that the mother had taken Thalidomide during the first trimester of her pregnancy, albeit it was difficult to pinpoint the precise time of drug exposure. The newborn experienced frequent episodes of vomiting, especially after feeding, in addition to the obvious limb abnormalities.

6. Root cause Analysis:

Serious foetal abnormalities may arise from exposure to thalidomide during pregnancy, especially between the 35th and 49th day following the mother's last menstrual cycle. According to studies, a single dose of the medication may be sufficient to cause teratogenic consequences in the growing foetus. The absence or underdevelopment of the ears and limbs, deafness, phocomelia, deformities of the face and cleft palate, and gastrointestinal system malformations are among the congenital problems linked to thalidomide exposure. Nearly 40% of affected newborns did not live past their first year of life, and many suffered from serious problems.[7,8]

7. Law and Regulatory Reforms Modifications for pregnant women's safety:

Category A: Sufficient research on expectant mothers has not revealed any danger to the growing foetus.

Category B: There is a lack of adequate and well-controlled research in pregnant women, however animal studies have not shown foetal injury.

Category C: Research on animals has shown detrimental effects on the foetus, but there is insufficient information on humans. If the anticipated therapeutic advantages outweigh the potential hazards, the medication may still be administered.

Category D: Medication may still be taken into consideration in severe or life-threatening situations where safer alternatives are not available, even though there is positive evidence of risk to the human foetus.

Category X: There is unmistakable proof of foetal malformations and risk, and the medication's likely risks exceed any potential advantages. As a result, using these medications while pregnant is not advised.

Frances Kelsey's (FDA) heroic role:

Thalidomide was never authorised for sale in the US, which helped avert a major public health emergency. Frances Kelsey voiced significant concerns about the inadequate evidence regarding the medicine's safety during the US Food and Drug Administration's evaluation of the drug application.[9] Her meticulous scientific evaluation and refusal to approve the medication in the absence of sufficient data were crucial in keeping thalidomide off the market in the US. The drug's b.i.d. for approval was withdrawn once thalidomide's harmful effects — particularly its capacity to cause serious birth defects — became publicly known. John F. Kennedy presented Dr. Kelsey with the President's Award for Distinguished Federal Civilian Service in recognition of her work to safeguard public health. Significant revisions to drug regulating laws were also brought about by the thalidomide catastrophe. The Kefauver-Harris Amendment, which gave the FDA more power to guarantee that medications were shown to be both safe and effective before being approved for public use, was one of the most significant developments in 1962.

8. Present Safety Environment:

The significance of "Package Inserts" and "Black Box Warnings":

The strictest safety alert for medications is a boxed warning, sometimes referred to as a black box warning. It is intended to educate the public and medical professionals about dangerous or potentially fatal drug dangers that could cause

serious injury or even death. The content of this warning is frequently organised in bullet points for ease of comprehension, and it is typically displayed in a boxed format with a bold, uppercase title. The written or printed document that comes with a pharmaceutical medication is called a medicine label, sometimes known as a package insert or product information leaflet. It includes crucial clinical and scientific data collected from studies and post-marketing experiences following the drug's release onto the market. This document's primary goal is to encourage the medication's safe and efficient use.[10]

9. Future Directions:

The primary reason for the reintroduction of thalidomide into contemporary clinical practice is its use in cancer treatment. It is now being investigated in clinical studies for the treatment of multiple myeloma and other cancers. Its efficacy as a stand-alone medication and in conjunction with other anticancer treatments is being assessed by researchers. Phase I, II, III, and IV are the four key phases of well-structured clinical trials that are used to evaluate such treatments. Phase 0 is an additional preparatory stage that has been added in recent years to enable extremely early evaluation of new medications prior to the start of extensive clinical trials.

B. THE SULFANILAMIDE ELIXIR TRAGEDY (1937):

Figure 4: The Tragic Sulfanilamide Elixir

1. Introduction of Drug:

The Bristol-based Massengill Company began selling a medication called sulfanilamide in 1937. This medication, which was created expressly to target and kill germs, was one among the first genuine antibiotics in the sulfa class. It was frequently used to treat both streptococcal infections in children and sexually transmitted infections in adults.

2. Background:

Many people found the initial sulfanilamide tablets to be uncomfortable to consume due to their extremely bitter taste. In order to facilitate administration, especially for youngsters and others who had trouble swallowing tablets, the business created a liquid formulation (an elixir) at the request of physicians and patients. A solvent that could both dissolve the medication and enhance its flavour was needed for the formulation. Diethylene glycol, a sweet-tasting liquid at room temperature that was later discovered to be extremely poisonous and capable of seriously harming the blood, kidneys, nervous system, and liver, was chosen for this reason.[11]

3. Pharmacology of Drug:

Sulfanilamide is a chemical made composed of an aniline structure connected to a sulfonamide group. In its protonated form, it has increased pharmacological efficacy. The potential for crystals to develop in the kidneys, which may increase toxicity, is one of its documented side effects. Sulfanilamide functions mechanistically by preventing bacteria from synthesising folic acid. It accomplishes this by blocking the enzyme pteridine synthetase, which is necessary for the synthesis of folic acid, and competing with para-aminobenzoic acid (PABA).

4. Occurrence of Adverse Drug Reaction:

About 240 gallons of Elixir Sulfanilamide were shipped to different regions of the US in October 1937. The American Medical Association (AMA) identified the first death instances associated with the product shortly after it was released. Six people had died after ingesting the elixir, according to an urgent telegram sent to the AMA Chemical Laboratory on October 11, 1937, by the president of the Tulsa County Medical Society in Oklahoma. In response, a sample of the product provided by the Massengill Company was examined by the AMA laboratory. Early research revealed that the solvent employed in the formulation—diethylene glycol—was the cause of the deaths rather than sulfanilamide itself.[11]

5. Nature of Tragedy:

The use of "Elixir Sulfanilamide" caused a terrible poisoning outbreak in the United States between September and October 1937, resulting in at least 73 verified deaths and several more suspicious cases. Fifteen states, from Virginia to California, reported these events. Before being released, the product had simply completed taste testing; human safety testing had not been conducted. It was sold from September 4 to October 15, 1937. By mid-October, the Food and Drug Administration received reports of deaths, including a telegram from Tulsa that listed nine fatalities.

6. Root Cause Analysis:

The poisonous solvent diethylene glycol used in the liquid formulation of "Elixir Sulfanilamide" was the cause of the deaths, not the otherwise safe and effective sulfanilamide medication itself. Within seven to twenty-one days, several victims—typically children receiving treatment for sore throats—developed serious symptoms such kidney failure, vomiting, abdominal discomfort, and convulsions. Diethylene glycol poisoning was nearly always fatal at the time because there was no known remedy or cure.

7. Law Changes and Regulatory Reforms:

The FDA, or Food and Drug Administration:

Officially, the action was filed under the misbranding accusation. The FDA claims that although the product included diethylene glycol and no alcohol at all, the term "elixir" misrepresented an alcoholic preparation. It wouldn't have broken the law if it had only been called a "solution," and the FDA wouldn't have had any solid legal justification to request its removal. An even greater disaster was probably averted by this loophole. The FDA's subsequent study emphasised how Massengill's inadequate safety testing and the intricacies of product naming were crucial in enabling the agency to intervene and recall the medication.[11]

8. Present Safety Environment:

Stronger procedures were created in the wake of the Sulfanilamide Elixir catastrophe to guarantee that medications are thoroughly tested before being made available to the general public. Before being approved by organisations like the Food and Drug Administration and the Central Drugs Standard Control Organization in India, medications must now pass several stages of clinical studies to evaluate their efficacy, safety, and proper dose. Pharmacovigilance helps identify uncommon or persistent side effects even after approval, guaranteeing prompt action against any possible hazards.

9. Future Directions:

After the Sulfanilamide Elixir tragedy, drug safety rules were significantly strengthened so that every medicine is properly tested for safety, including both its active ingredients and the substances used to prepare it, before it is approved. At the same time, stricter regulations, better manufacturing standards, and ongoing monitoring after marketing were introduced to quickly detect and respond to any harmful effects once drugs are in use.

C. THE DIETHYLSTILBESTROL TRAGEDY (1971):

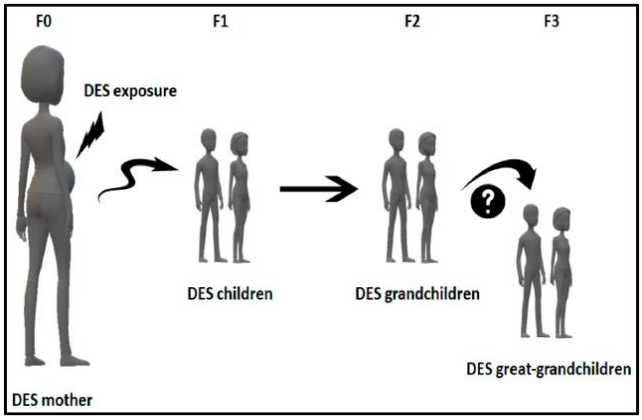

Figure 5: Mother-to-Child Exposure to DES

1. Introduction of Drug:

Between 1938 and 1971, the United States made extensive use of diethylstilbestrol (DES), a synthetic, nonsteroidal version of oestrogen. In an attempt to prevent miscarriages and lessen other pregnancy-related difficulties, particularly when there were indications of possible pregnancy loss, it was recommended to expectant mothers.

2. Background:

One synthetic oestrogen that can be consumed orally is diethylstilbestrol (DES). It was first thought to help lower the incidence of spontaneous abortion, but subsequent studies revealed that it had no discernible effect on preventing miscarriage.[12]

3. Pharmacology of Drug:

In the body, synthetic non-steroidal oestrogens function similarly to natural oestrogen. They were believed to help sustain pregnancy and lower the risk of miscarriage by increasing uterine blood flow, supporting the uterine lining, and lessening uterine contractions. These medications, which are well absorbed when taken orally, were formerly used to treat menopausal symptoms, avoid preterm labour, and recurrent miscarriages.

4. Occurrence of Adverse Drug Reaction:

Barker and Trichopoulos[12] proposed in the early 1990s that the risk of diseases including breast cancer and cardiovascular disease may start to manifest as early as foetal life. According to Barker's theory, inadequate prenatal nutrition and low birth weight may "program" metabolic alterations in the foetus, raising the risk of heart disease in later life. Subsequent research also revealed that DES exposure during pregnancy was associated with an increased risk of uncommon vaginal and cervical cancers, including clear cell carcinoma. This was followed by an increased risk of breast cancer in women who had taken the medication, as well as worries about comparable risks in those exposed prior to birth.[13]

5. Nature of Tragedy:

Diethylstilbestrol (DES), a synthetic oestrogen, was provided to almost 4 million American women between 1938 and 1971 in an attempt to improve pregnancy outcomes. But by 1953, it was evident that the medication did not genuinely stop miscarriages or other problems. Subsequent research connected DES exposure to an increased risk of breast cancer in women who used it, as well as uncommon malignancies of the cervix and vagina in their unborn daughters.[14]

Daughters exposed to diethylstilbestrol during pregnancy:

It was later shown that daughters exposed to diethylstilbestrol (DES) during pregnancy were more likely to develop clear cell adenocarcinoma of the cervix and vagina. Although few cases have been observed in women in their 30s and 40s, this uncommon cancer typically manifests between the ages of 17 and 22. Researchers are still keeping an eye on these people because they fear that as this demographic ages, there may be another spike in instances.[14]

6. Root Cause Analysis:

When a pregnant woman used DES, the medication passed through the placenta and exposed the growing fetus—particularly female fetus—to high quantities of synthetic oestrogen, which interfered with normal reproductive development. Later research has connected this in-utero exposure to a somewhat elevated incidence of breast cancer in female children. Inadequate drug testing, unregulated usage during pregnancy, and a lack of awareness about the long-term effects of DES were major contributing factors to the tragedy.

7. Law Changes and Regulatory Reforms:

The Food and Drug Administration's Function in Patient Safety-

Due of its association with clear cell adenocarcinoma in daughters exposed prior to birth, the U.S. Food and Drug Administration issued a warning against the use of diethylstilbestrol during pregnancy in 1971. Drug regulations were significantly altered as a result of this disaster, requiring producers to present convincing proof of both efficacy and safety before any medication could be authorised for use.[14]

The USFDA established the Pregnancy and Lactation Labelling Rule:

The FDA makes ensuring that vaccines and prescription medications are clearly labelled with correct scientific information about how to use them safely. Additionally, this material must not be deceptive or predicated on unsubstantiated assertions. The Physician Labelling Rule (PLR), which was implemented by the government in 2006, revised the format and presentation of information about biological products and prescription drugs.[15]

8. Kefauver-Harris Amendments of 1962:

In response to grave concerns about drug safety brought up by incidents such as the Thalidomide tragedy and the Diethylstilbestrol experience, the Kefauver–Harris Amendments were introduced in the United States. Along with tighter regulation of clinical trials, patient consent, and drug marketing, they mandated that pharmaceutical companies prove both safety and efficacy prior to approval. This signalled a significant change toward more stringent FDA regulation and improved public health protection.

9. The Safety Ecosystem of Today:

CDSCO, or the Central Drugs Standard Control Organization-

Drug safety in India is governed by the Central Drugs Standard Control Organization (CDSCO), which works under the Ministry of Health and Family Welfare. It helps pharmacovigilance systems to track adverse effects and guarantees that producers adhere to Good Manufacturing Practices (GMP). Additionally, CDSCO helps to protect the safety, efficacy, and dependability of healthcare items in the nation by issuing safety alerts on prohibited drugs, medical equipment, and quality issues including inferior or counterfeit medications.[16,17]

10. Future Directions:

It has been discovered that millions of women in the US, Europe, and Australia who were exposed to DES prior to birth are roughly twice as likely to get breast cancer as those who were not. Additionally, daughters, granddaughters, and even great-granddaughters may be impacted by this elevated risk. These days, long-term health monitoring and patient safety are the main concerns with DES rather than its usage as a medication. It is recommended that those who are exposed to it get frequent examinations in order to identify potential malignancies or reproductive issues early. Stricter rules from organisations like the U.S. Food and Drug Administration and increased public awareness aim to ensure safer medication use, particularly during pregnancy, and prevent similar tragedies in the future. Global health systems, including those supported by the World Health Organization, now assist in tracking adverse drug effects.

CLINICAL TRIAL PHASES:

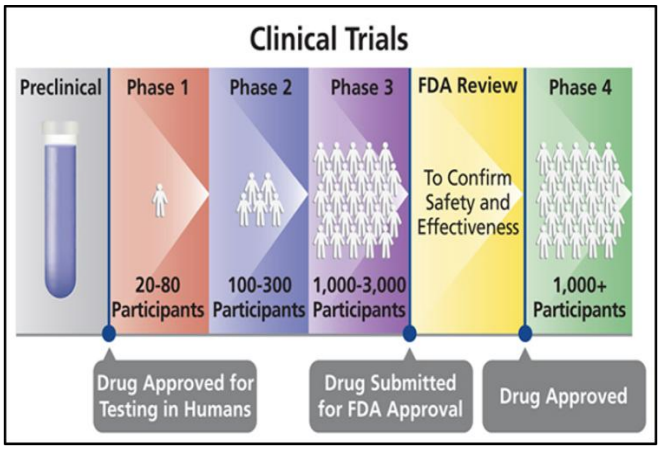

Figure 6: Clinical Trial Phases

FUTURE OUTLOOK IN PREVENTION OF ADVERSE DRUG REACTIONS:

With the aid of cutting-edge technology and increased international collaboration, the prevention of adverse medication responses is anticipated to greatly improve in the future. Digital reporting, real-world data, and artificial intelligence are already being used by programs like India's Pharmacovigilance Programme and global systems backed by the World Health Organization to detect drug safety problems early. However, personalised medicine — including genetic testing — may be able to forecast a person's sensitivity to a particular medication, lowering the possibility of negative side effects. Drug safety is expected to become more proactive and dependable in the next years with tighter restrictions, more patient knowledge, and ongoing monitoring.

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