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Review Article

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REVIEW ON NITROFURAN DERIVATIVE; NITROFURANTOIN INDUCED NEUTROPENIA AND AGRANULOCYTOSIS; IT'S TREATMENT GOALS

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Abstract

Neutropenia is a clinical condition characterized by a reduced number of neutrophils, a type of white blood cell essential for defending the body against infections. It can occur due to chemotherapy, certain medications, autoimmune diseases, or bone marrow disorders. Nitrofurantoin, a nitrofuran derivative widely used for the treatment and prevention of uncomplicated urinary tract infections, has been rarely associated with severe hematological reactions such as neutropenia and agranulocytosis. These reactions result in increased susceptibility to infections and may become life-threatening if not promptly managed. Treatment of neutropenia primarily depends on its cause and severity. Pharmacological management includes colony-stimulating factors such as granulocyte colony-stimulating factor (G-CSF) drugs—filgrastim and pegfilgrastim—which stimulate bone marrow to produce neutrophils. In autoimmune cases, corticosteroids like prednisone are used to suppress immune-mediated destruction of neutrophils, while immunosuppressants such as cyclosporine or methotrexate are prescribed for chronic or severe cases. Febrile neutropenia requires immediate broad-spectrum antibiotics, with antifungal or antiviral agents added as necessary. Non-pharmacological measures involve discontinuing the causative drug, maintaining strict hygiene, ensuring a balanced diet, and regular blood count monitoring to assess recovery. Early detection, effective management, and awareness of drug-induced neutropenia can significantly reduce complications and improve patient outcomes. Advances in therapeutic strategies and infection control have enhanced the survival and quality of life of patients affected by this rare adverse effect.

Keywords: Neutropenia, Agranulocytosis, Granulocyte colony-stimulating factor (G-CSF), filgrastim, Corticosteroids, Antibiotic therapy, Bone Marrow.

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Introduction

The Nitrofurantoin antibiotics were used to treat bacterial infections in livestock. They have been banned in many jurisdictions over concerns of carcinogenic residues in

edible tissue. There are four parent compounds that comprise the nitrofurantoin class: furazolidone, furaltadone, nitrofurazone, and nitrofurantoin. They are all broad-spectrum antibiotics that contain a 5-nitrofurantoin ring structure [2]. The parent nitrofurantoin are rapidly metabolized to protein-bound metabolites, so the use of

the parent drugs as marker residues is ineffective; however, the tissue-bound metabolites are stable in the body for several weeks after treatment and thus represent a better choice as marker residues [3].

IUPAC Name: 1-[[[(5-nitrofuran-2-yl) methylidene] amino]imidazolidine-2,4-dione

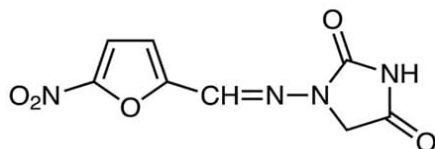


Fig 01: Nitrofurantoin

Nitrofurantoin

Nitrofurantoin is an antibiotic medication that is used for the treatment of uncomplicated lower urinary tract infections. It is effective against most gram-positive and gram-negative organisms. Nitrofurantoin's primary use has remained in treating and prophylaxis of urinary tract infections. Nitrofurantoin is recommended as a first-line agent for uncomplicated cystitis because of efficacy against common uropathogens and relatively low resistance rates. Nitrofurantoin is a prescription antibiotic and used to treat and prevent uncomplicated low urinary tract infection. It causes the neutropenia [4].

Side Effects

- diarrhoea that is watery or bloody;
- sudden chest pain or discomfort, wheezing, dry cough or hack;
- new or worsening cough, trouble breathing;
- fever, chills, body aches, tiredness, unexplained weight loss;
- numbness, tingling, or pain in your hands or feet;
- liver problems--nausea, upper stomach pain, itching, tired feeling, loss of appetite, dark urine, clay-coloured stools, jaundice (yellowing of the skin or eyes)
- lupus-like syndrome--joint pain or swelling with fever, swollen glands, muscle aches, chest pain, vomiting, unusual thoughts or behaviour, and patchy skin colour.
- Nitrofurantoin is a nitrofuran derivative:

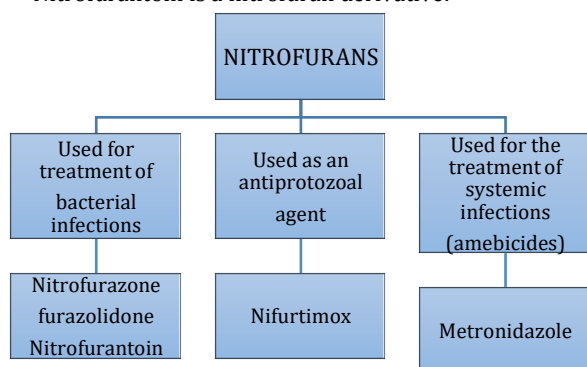


Figure 02: Image of uses of Nitrofurans

Mechanism of Action

Nitrofurantoin is an antibacterial agent specific for urinary tract infection and is bactericidal in urine at therapeutic doses. The mechanism of the antimicrobial action of nitrofurantoin is unusual. Nitrofurantoin is reduced by bacterial flavoproteins to reactive intermediates which alter bacterial ribosomal proteins, and other macromolecules. As a result of such inactivation's, the vital biochemical processes of protein synthesis, aerobic energy metabolism, DNA synthesis, RNA synthesis, and cell wall synthesis are inhibited.

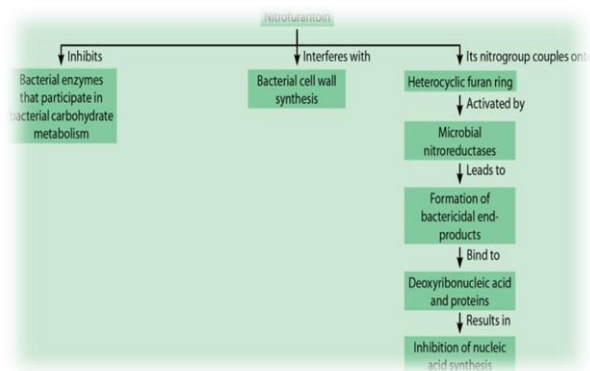


Figure 3: Mechanism of Action of Nitrofurans

Adverse Effects

Nitrofurantoin may impart a dark yellow or brown color to the urine of patients receiving the drug. Other adverse effects reported rarely with the drug include crystalluria, photosensitization, angioedema, anaphylaxis, eosinophilia, increases in serum inorganic phosphorus concentrations, back pain, rhinitis, fever, and asthmatic attacks in patients with a history of asthma. Nitrofurantoin has been associated with parotitis in at least one patient [5].

UTI Dosing

The dose of this medicine will be different for different patients. Follow your doctor's orders or the directions on the label. The amount of medicine that you take depends on the strength of the medicine. Also, the number of doses you take each day, the time allowed between doses, and the length of time you take the medicine depend on the medical problem for which you are using the medicine.

For Oral Dosage Forms (Capsules and Tablets)

For prevention of urinary tract infections

- Adults-50 to 100 milligrams (mg) at bedtime.
- Children 1 month of age and older-Dose are based on body weight and must be determined by your doctor.
- Children younger than 1 month of age-Use is not recommended.

For treatment of urinary tract infections:

- Adults-50 to 100 milligrams (mg) 4 times a day.
- Children 1 month of age and older—Dose is based on body weight and must be determined by your doctor.
- Children younger than 1 month of age-Use is not recommended.

For Oral Dosage Form (Extended-Release Capsules)

- For treatment of urinary tract infections:
- Adults and children 12 years of age and older- 100 milligrams (mg) every 12 hours for 7 days.
- Children younger than 12 years of age-Use and dose must be determined by your doctor.

For Treatment of Urinary Tract Infections

- Adults and children weighing 40 kilograms (kg) or more-50 to 100 milligrams (mg) 4 times a day.
- Children 1 month of age and older-Dose are based on body weight and must be determined by your doctor. The dose is usually 5 milligram per kilogram (mg/kg) of body weight or 7 mg/kg of body weight per 24 hours given in 4 divided doses.

Table 1: Contraindications of Nitrofurantoin.

CONTRAINDICATION	
NITROFURANTOIN	
Nitrofurantoin should not be given to patients with hepatotoxicity or cholestatic jaundice history.	Do not take Macrobid if you have severe kidney disease.
Contraindicated in patients with renal dysfunction.	Macrobid is contraindicated in patients with history of hepatotoxicity.
Administration of nitrofurantoin is contraindicated in patients and neonates with G6PD deficiency.	Contraindicated in patients with renal dysfunction and G6PD deficiency.
Drug/Medication Interaction	
NITROFURANTOIN	
Cholera vaccine : Avoid administration	Chloroprocaine: chloropropane and Macrobid can cause oxygen deprivation in vital tissues and organs of the body.
Darolutamide: Increases the level of nitrofurantoin	Etidocaine: Etidocaine is also a local anesthetic that can cause methemoglobinemia
Leflunomide: Increases the risk of liver problems.	Prilocaine: Close supervision is necessary when using prilocaine, and Macrobid are used together.
Food/Beverage/Supplement Interactions	
NITROFURANTOIN	
There no food or drinks that u must avoid when taking nitrofurantoin.	Avoid spicy food or coffee and alcohol to prevent stomach irritation

Indication:

- Urinary tract infection -treatment and prophylaxis.
- Vesico-ureteric reflex- conservative treatment.

Urinary tract infection

Among the universal infectious diseases which increase the economic burden on the society, Urinary tract infection is the most common one. A urinary tract infection (UTI) is a disease that influence organs concerned to the urinary system i.e. ureter, bladder,

urethra along with kidney. Infections mainly occur in the lower urinary tract i.e. in the urinary bladder along with the urethra.

Contraindications for nitrofurantoin use

Nitrofurantoin should not be administered in the following situations:

1. Impaired Kidney Function

The medication is contraindicated in patients with significant renal dysfunction, including anuria, oliguria, or severely reduced creatinine clearance (less than 30 mL/min), as this may lead to drug

accumulation and increase the risk of adverse effects. Though traditionally avoided below a creatinine clearance of 60 mL/min, recent recommendations suggest cautious use when CrCl is 30 mL/min or higher.

2. Pregnancy and Newborns

Nitrofurantoin should not be used in pregnant women nearing delivery (38–42 weeks gestation), during active labor, or when labor is expected soon, due to the potential for hemolytic anaemia in the newborn. It is also contraindicated in infants under one month old for the same reason.

3. G6PD Deficiency and Oxidant Sensitivity

Individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency or known sensitivity to oxidative agents are at increased risk of haemolytic anaemia, and nitrofurantoin should be avoided in such cases.

4. Allergic Reactions

Patients with a known allergy to nitrofurantoin or any of its components should not be treated with this medication.

5. Previous Liver Issues Related to Nitrofurantoin:

The drug is also contraindicated in those who have previously experienced cholestatic jaundice or liver dysfunction following nitrofurantoin therapy.

Dose Recommendations:

Treatment of Urinary Tract Infections (UTIs)

- Age Group: Children aged 1 month to 12 years
- Dosage: 5 to 7 mg/kg/day, taken orally and divided into four equal doses
- Treatment Duration: 7 days
- Maximum daily dose: 400 mg

Prevention of UTIs (Prophylaxis)

- Dosage: 1 to 2 mg/kg per day, given either once at bedtime or in two divided doses
- Maximum dose per 24 hours: 100 mg

Adverse Drug Reaction

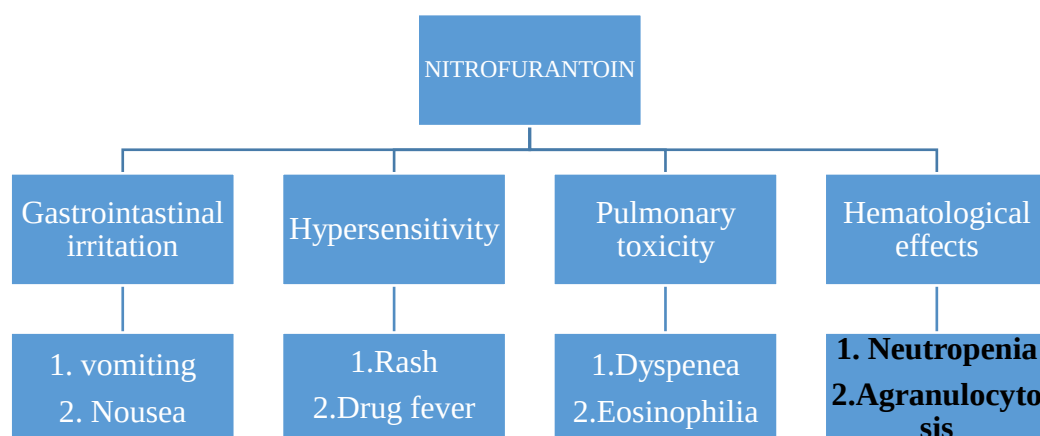


Figure 4: Adverse Drug Reaction of Nitrofurantoin.

Neutropenia

- ✓ Neutropenia is defined as an absolute neutrophil count (ANC) below 1500 cell/ml.
- ✓ Neutropenia is a reduction in the absolute neutrophil count (ANC) in the peripheral blood [7].

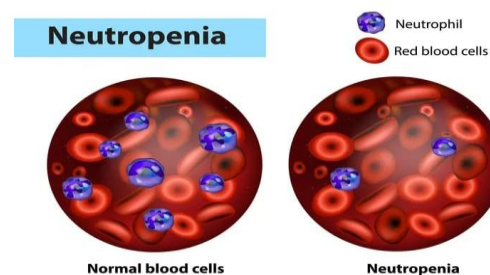


Figure 5: Image of Neutropenia.

Neutropenia refers to lower – than normal level of neutrophils in blood. A neutrophil is a type of white blood cell that your bone marrow primarily makes. White blood

cell is general, and neutrophils in particular fight in your body. An absolute neutrophil count (ANC) of less than 1500 per microliter (1500\ micro-L). Neutropenia is defined as less than 500 per microliter (500\micro-L).

The Range Of Neutrophils is

- ✓ Mild neutropenia: 1,000 – 1,500
- ✓ Moderate neutropenia :500 -1,000
- ✓ Severe neutropenia: Less than 500.
- Nitrofurantoin is a prescription antibiotic and used to treat and prevent uncomplicated low urinary tract infection. It can cause neutropenia.

Types of neutropenia

- Congenital neutropenia
- Idiopathic neutropenia
- Cyclic neutropenia
- Auto immune neutropenia.

Epidemiology

Neutrophils play a primary role in the immune defense against extracellular bacteria, including Staphylococci, Streptococci, and Escherichia coli, among others. They also protect against fungal infections, including those produced by Candida albicans. Once the neutrophil count is below $1.5 \times 10^9/L$, recurrent infections become more common. The monocyte count may increase as a compensatory mechanism. Neutropenia can be considered acute (<3 months) or chronic (>3-6 months). Neutropenia should be evaluated in conjunction with the bone marrow response which also helps clarify the pathophysiology. Circulating neutrophils account for only 3% to 5% of the total, with the remainder sequestered until activated by infection or another stimulus. The clinical significance of this is that even in cases of peripheral neutropenia if bone marrow reserves are adequate, the infectious risk may be mitigated. Neutropenia can be classified by decreased bone marrow reserves (primary) or normal bone marrow reserves (secondary) [8].

Decreased Bone Marrow Reserves

Decreased bone marrow reserves cause an initial lack of availability of neutrophils and precursor cells. This can be related to intrinsic or extrinsic factors.

- Intrinsic factors include genetic mutations (e.g., ELANE, HAX1, WAS mutations) or acquired myelodysplastic syndrome, and causes vary by age.
- Extrinsic factors limiting neutrophil production can be related to 2 main causes:
 - physical bone marrow infiltration/replacement/restriction-e.g., leukaemia, neuroblastoma, or osteopetrosis
 - external limiting factors
 - Viral or bacterial infections, radiation, drug-induced, alcoholism
 - Nutritional deficiencies of folate, vitamin B12, and copper [9].

Normal Bone Marrow Reserves

Normal bone marrow reserves are common and provide the availability of neutrophils, which are then either destroyed, sequestered, consumed, or ineffectively transported/non-functional.

Genetic causes of neutropenia usually affect neutrophil chemotaxis or function. The pathophysiology section will describe the most common genetic syndromes. Ineffective neutrophil trafficking and function can be affected at many steps. The primary causes of defective neutrophil function include failure of the following mechanisms:

- Migration into inflammation sites (abnormal chemotaxis)
- Adherence to endothelial cells
- Ingestion of bacteria
- Production of microbicidal compounds and toxic reactive oxygen species to kill pathogens
- Formation of phagolysosomes [10].

Drugs can cause both hypoplastic neutropenia from bone marrow suppression and autoimmune neutropenia [11]. Chemotherapeutic agents are commonly known to cause neutropenia. Levamisole is a veterinary antiparasitic drug that has been frequently used as an adulterant in cocaine and is known to cause agranulocytosis [12]. Other common drugs known to cause neutropenia include the following [13]:

- Aminopyrine
- Cephalosporins
- Dapsone
- Heavy metals (e.g., arsenic, aluminium phosphate) [ix]
- Hydroxychloroquine
- Hydralazine
- Lamotrigine
- Methimazole
- Oxacillin/penicillin's
- Phenothiazine
- Procainamide
- Propylthiouracil
- Quinidine/quinine
- Rituximab
- Sulfasalazine
- Sulphonamides
- Trimethoprim-sulfamethoxazole
- Vancomycin
- Clozapine

Clozapine is an antipsychotic used for treatment-resistant psychosis and has been underutilized in part due to adverse effects, including severe neutropenia and agranulocytosis (occurring in 3.8% and 0.9% of patients, respectively), requiring stringent hematologic monitoring. [14, 15]. The significance of neutropenia is that usage is often avoided despite clozapine being the current most effective treatment for treatment-resistant schizophrenia. A genetic predisposition to developing agranulocytosis is likely involved, and this is an area needing further study [16, 17]. Rechallenge with clozapine is possible in selected cases. Please see Stat Pearls' associated review on "Clozapine" for further details.

Autoimmune or anti-neutrophil neutropenia is a common cause of neutropenia. However, autoantibody levels do not closely correlate with the degree of neutropenia. A positive antinuclear antibody (ANA) is suggestive, but not definitive, of autoimmune neutropenia. Both immunoglobulin (B-cell) and cell-mediated (T-cell, natural killer cell) immunity can be involved. Autoimmune destruction can occur in the bone marrow or peripherally, primarily through monocyte/macrophage elimination via the spleen.

Autoimmune neutropenia in infancy occurs due to antineutrophil antibodies and generally has a benign course; this condition spontaneously resolves about 90% of the time within 2 to 3 years of onset. [18] Autoimmune neutropenia's are more common in adult women, especially those who are between 25 and 40. Symptoms of connective tissue diseases like lupus and Sjögren syndrome are common. Felty syndrome is a classic example of autoimmune neutropenia characterized by chronic rheumatoid arthritis, splenomegaly, and activated large granular lymphocytes. Autoimmune destruction of neutrophils has also been observed in these conditions:

- Thyroid disease
- Inflammatory bowel disease
- Chronic autoimmune hepatitis
- Granulomatosis with polyangiitis
- Hodgkin lymphoma
- Infections
- Hepatitis B and C (although these can acutely cause neutropenia, they are more commonly associated with a chronic immune-mediated form)

Increased consumption of neutrophils is common in sepsis and bacterial infections. Neonates are especially prone to neutropenia from sepsis.

Idiopathic neutropenia, where no cause can be found despite extensive investigation, is common. Results from one study of patients with neutropenia found no identifiable cause in 48% of patients. Cell-mediated immunity may be an underlying pathology of chronic idiopathic neutropenia through mediation by myeloid-derived suppressor cells, which is an emerging area of study.

Agranulocytosis

Agranulocytosis gets its name from "granulocyte." Granulocytes are white blood cells that contain enzymes that kill germs and break down substances that may harm your body. There are three types of granulocytes: neutrophils, eosinophils and basophils. Most of your body's white blood cells are neutrophils. This is why healthcare providers check neutrophil levels to diagnose agranulocytosis. Agranulocytosis is rare life-threatening adverse reaction characterized by an absolute neutrophil count <500 cell/mL of blood. Almost complete absence of neutrophils (ANC <100 -200/mL, or <500/mL with sepsis).

- Represent most extreme form of neutropenia.
- Recent improvement, the molarity rate for idiosyncratic drug-induced agranulocytosis remains high, mostly due to the high rate of infectious complication.
- All agranulocytosis cases are severe neutropenia, but all neutropenia progresses to agranulocytosis.[19]

There are two types of agranulocytosis.

- **Inherited Agranulocytosis** results from a genetic disorder that affects how your body makes neutrophils. It's more common among babies and children.
- **Acquired Agranulocytosis** can have many causes but is usually a medication side effect (up to 70% of agranulocytosis cases). This form of agranulocytosis appears most often in adults.

Agranulocytosis

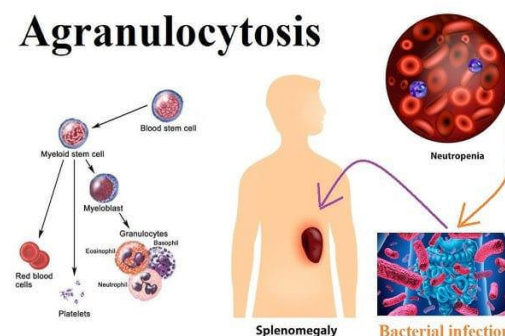


Figure 6: Life Cycle of Agranulocytosis

Symptoms

Agranulocytosis causes symptoms of infection that may appear suddenly or gradually. Symptoms may include:

- Fever and chills.
- Faster heart rate and breathing.
- Muscle weakness and fatigue.
- Sore throat (pharyngitis) and bleeding, inflamed gums.
- Sores in your mouth and throat that make it difficult to swallow.
- Sudden low blood pressures (hypotension), which can make you feel lightheaded or weak, or cause you to pass out.

Risk Factors

It's slightly more common in women. People of all ages can experience agranulocytosis.

Agranulocytosis is more common among people who:

- Are receiving chemotherapy treatments for cancer.
- Have autoimmune diseases (conditions that cause your immune system to attack part of your own body) such as lupus or rheumatoid arthritis.
- Take certain prescription drugs, such as the antipsychotic clozapine (Clozaril®), the antibiotic trimethoprim/sulfamethoxazole (Bactrim™).

Goals of Treatment

Goals

1. Identify and eliminate the underlying cause

Goals

- Stop further destruction or suppression of neutrophils and agranulocytosis.

Action:

- Discontinue offending drug

Eg: Nitrofurantoin, Clozapine, Methimazole etc.,

2. Prevent and treat infections

Goal: Reduce infection risk and control existing infection promptly.

Action

- Use antifungal/ antiviral therapy.
- Maintain strict aseptic precaution.

3. Supportive and Nutrition care

Goal: Maintain overall immune body strength.

Action

- Provide high- protein diet.
- Take balanced diet rich in vitamin B12.
- Avoid raw/ undercooked food.

4. Monitor and follow up

Goal: Take recovery and prevent recurrence.

Action:

- Perform regular and CBC to monitor neutrophil.

5. Manage severe/ persistent care

Goal: Prevent life-threatening complication.

Action:

- Hospitalization in care of severe agranulocytosis.

Non-Pharmacological Treatment

1. Infection Prevention and Control

a. Isolation and protective environment

Patients with severe neutropenia (ANC < 500 cells/μL) should be placed in protective isolation to minimize exposure to potential pathogens. The environment should be clean, well-ventilated, and free from flowers or stagnant water that may harbour microorganisms. Visitor access should be restricted, and anyone entering should practice strict infection-control measures such as gowning and hand hygiene [20-21].

b. Hand Hygiene

Frequent hand washing with antiseptic soap or alcohol-based sanitizer is the single most effective method to prevent infection transmission. Health-care workers and caregivers must perform hand hygiene before and after any patient contact [22].

c. Environmental Hygiene

Surfaces, medical devices, and bed rails should be disinfected regularly to reduce contamination risk. Patients should avoid close contact with individuals who have infectious illnesses such as colds or influenza [23].

2. Nutritional Management

A neutropenic diet (low-bacteria diet) is recommended to reduce exposure to food-borne pathogens. Raw or undercooked meat, fish, eggs, and unpasteurized milk products should be avoided. All fruits and vegetables should be thoroughly washed and, when possible, peeled or cooked before consumption. Adequate intake of proteins, vitamins (B12, folate), and minerals (zinc, iron) supports bone-marrow recovery. Patients should drink only boiled or bottled water to avoid contamination [24].

3. Oral and Skin Care

Regular oral hygiene helps prevent mucosal breakdown and bacterial colonization. Patients should use a soft toothbrush and rinse with mild saline or chlorhexidine mouthwash. Alcohol-based mouthwashes should be avoided as they may cause mucosal irritation. Daily skin inspection for cuts or rashes is advised, as damaged skin can act as a portal of infection. Patients should avoid shaving with blades; instead, use an electric razor to minimize skin injury [25].

4. Lifestyle and Activity Modifications

Patients should avoid crowded public places and wear protective masks when in hospital or outdoors during periods of neutropenia. Adequate rest and sleep are essential to support immune recovery. Constipation should be prevented to reduce the risk of rectal tears and infections-encouraging high-Fiber diets and fluids. Rectal thermometers, enemas, and suppositories must be avoided to prevent mucosal injury [26].

5. Monitoring and Early Detection

Daily monitoring of body temperature is essential; any fever > 38 °C should be reported immediately. Regular complete blood count (CBC) monitoring helps assess recovery of neutrophils. Patients and caregivers must be educated to recognize early infection signs such as sore throat, cough, dysuria, or redness at IV sites.

6. Psychological and Social Support

Long-term neutropenia often leads to anxiety and social isolation; hence, psychological counselling is beneficial. Providing emotional support and patient education improves adherence to infection-prevention measures. Family and peer support groups also help patients cope with stress and fear of infection [27].

7. Vaccination and Prophylaxis

Live vaccines should be avoided during active neutropenia or immunosuppression due to infection risk. Inactivated vaccines such as influenza and pneumococcal should be administered before chemotherapy or once neutrophil counts recover. Family members and caregivers should also be vaccinated to minimize transmission.[28]

➤ Pharmacological Treatment

(a) Colony-Stimulating Factors (CSFs)

Granulocyte Colony-Stimulating Factor (G-CSF)

Drug: filgrastim, Pegfilgrastim, Lenograstim

Mechanism of Action: G-CSF binds to receptors on hematopoietic stem cells, stimulating proliferation, differentiation, and activation of neutrophil precursors, leading to increased production and release of mature neutrophils.

Indications

- Chemotherapy-induced neutropenia
- Congenital and cyclic neutropenia
- Bone marrow transplantation
- Severe chronic neutropenia

Dosage

- Filgrastim: 5 µg/kg/day subcutaneously or intravenously until ANC > 10,000/µL
- Pegfilgrastim: 6 mg subcutaneously once per chemotherapy cycle

Adverse Effects

- Bone pain
- Fever
- Splenomegaly (rare)

Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF)

Drug: Sargramostim

Mechanism: Stimulates proliferation of granulocytes, monocytes, and macrophages.

Indications: Post bone marrow transplantation, myelodysplastic syndromes.

Adverse Effects: Fever, malaise, edema, bone pain.[29]

(b) Corticosteroids

Drugs: Prednisone, Prednisolone

Mechanism of Action: Suppress immune-mediated destruction of neutrophils and reduce inflammation in autoimmune neutropenia.

Dosage: Prednisone 0.5–1 mg/kg/day orally.

Uses: Autoimmune neutropenia, systemic lupus erythematosus-associated neutropenia.

Adverse Effects: Weight gain, hypertension, hyperglycaemia, increased infection risk [30].

(c) Immunosuppressive Agents

Drugs: Cyclosporine, Azathioprine, Methotrexate.

Mechanism: Suppress abnormal immune responses that lead to neutrophil destruction.

Uses: Severe chronic autoimmune neutropenia unresponsive to corticosteroids.

Adverse Effects: Nephrotoxicity, hepatotoxicity, immunosuppression [31].

(d) Antibiotic and Antifungal Therapy

Patients with febrile neutropenia (fever >38°C with ANC <500/µL) require immediate empirical antimicrobial therapy.

Empirical Antibiotic Therapy

- Piperacillin–Tazobactam
- Cefepime or Ceftazidime
- Carbapenems (Meropenem, Imipenem)

If MRSA is suspected, add Vancomycin or Linezolid.

Antifungal Prophylaxis: Fluconazole, Posaconazole, or Amphotericin B in prolonged neutropenia (>7days).

Antiviral Therapy

- Acyclovir for herpes simplex or varicella-zoster infections [32].

(e) Hematopoietic stem cell transplantation:

For patients with severe congenital neutropenia or those who do not respond to G-CSF therapy.

Outcome: Offers potential cure but associated with high risk and cost [33].

Conclusion

Nitrofurantoin, a commonly used antibiotic for urinary tract infections, can rarely cause serious hematological complications such as neutropenia and agranulocytosis. These conditions result from a marked reduction in neutrophils, leading to increased vulnerability to bacterial and fungal infections. Early recognition of drug-induced neutropenia is crucial for preventing life-threatening complications. The main goals of treatment include prompt discontinuation of the causative drug, stimulating bone marrow recovery using granulocyte colony-stimulating factors (such as filgrastim or pegfilgrastim), and managing infections with appropriate antibiotics. Supportive care-such as maintaining hygiene, monitoring blood counts, ensuring good nutrition, and providing psychological support-also plays a key role in recovery. Overall, awareness among clinicians and patients about this rare but serious adverse effect of nitrofurantoin can help in timely diagnosis and management, thereby improving patient safety and treatment outcomes.

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Conflicts of Interest

The authors declare no conflicts of interest.

Author Contribution

Both are contributed equally

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Ethical Considerations and Inform Consent

Not Applicable

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