# Drug-induced blood disorders

# in ICU patients

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Partial fulfillment of master degree of Intensive Care

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**2010**

# الإضطرابات الدموية الناتجة عن العقاقير
# في مرضى الرعاية المركزة

**رسالة توطئة**

للحصول على درجة الماجستير في الرعاية المركزة

**مقدمة من**

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2010

# Acknowledgement

First and foremost, thanks to ALLAH, the most merciful and the greatest beneficent.

I would like to express my great appreciation to Prof. Dr. Sherif Wadie Nashed, Professor of Anesthesiology and Intensive care, Faculty of Medicine, Ain Shams University; for his sincere effort, valuable advice and great confidence that he gave me throughout the whole work. His time and supreme effort are clear in every part of this work.

I am deeply grateful to Dr. Ayman Anes Metry, Lecturer of Anesthesiology and Intensive care, for his great directions all through the work & continuous advice.

I would like to express my appreciation to Dr. George Mekhael Khalel, Lecturer of Anesthesiology and Intensive care, for his meticulous supervision and efforts to complete this work.

Finally no words can express the warmth of my feelings to my family both current and future, to whom I am forever indebted for their patience, support and help.

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# Abbreviations

| | |
|---|---|
| 2,3-BPG | 2,3-bisphosphoglycerate |
| AA | Aplastic anemia |
| ACA | Anticardiolipin antibody |
| ACCP | American College of Chest Physicians |
| ACT | Activated clotting time |
| AED | Antiepileptic drugs |
| AHF | Antihemophilic factor |
| AIDS | Acquired immune deficiency syndrome |
| AIHA | Autoimmune hemolytic anemia |
| ANC | Absolute neutrophil count |
| AP | Antiplasmin |
| APC | Activated protein C |
| APS | Antiphospholipid antibody syndrome |
| ASA | Acetylsalicylic acid |
| ASH | American Society of Hematology |
| ATG | Antithymocyte globulin |
| BMT | Bone marrow transplantation |
| BUN | Blood urea nitrogen |
| CB | Cord blood |
| CDI | Clinically documented infection without microbiological evidence. |

| | |
|---|---|
| CFU-E | Colony forming unit-erythrocyte |
| CKD | Chronic kidney disease |
| CLCr | Creatinine clearance |
| CMV | Cytomegalovirus |
| COX-2 | Cyclooxygenase-2 |
| CS | Corticosteroids |
| CsA | Cyclosporine A |
| CY | Cyclophosphamide |
| CYP | Cytochrome P-450 |
| DAT | Direct antiglobulin test |
| DIAG | Drug-induced Agranulocytosis/Neutropenia |
| DIC | Disseminated intravascular coagulation |
| DIHA | Drug-induced immune hemolytic anemia |
| DIHS | Drug-induced hypersensitivity syndrome |
| DINP | Drug-induced neutropenia |
| DISS | Drug-induced Sweet's syndrome |
| DIT | Drug-induced immune thrombocytopenia |
| DNA | Deoxyribonucleic acid |
| DRESS | Drug rash with eosinophilia and systemic symptoms |
| DTI | Direct thrombin inhibitor |
| DVT | Deep vein thrombosis |
| EBV | Epstein-Barr virus |

| | |
|---|---|
| ECT | Ecarin clotting time |
| EDTA | Ethylenediaminetetraacetic acid |
| EIA | Enzyme-linked Immunoassay |
| ESA | Erythropoiesis-stimulating agent factor |
| F VIII | Factor VIII |
| FDA | Food and Drug Administration |
| FDP | Fibrinogen degradation products |
| FFP | Fresh frozen plasma |
| FUO | Fever of unknown origin |
| G6PD | Glucose-6-phosphate dehydrogenase deficiency |
| GAGs | Glycosaminoglycans |
| G-CSF | Granulocyte-colony stimulating factor |
| GM-CSF | Granulocyte/macrophage colony stimulating |
| GPIb | Glycoprotein Ib |
| GPIIb/IIIa | Glycoprotein IIb/IIIa |
| GSSG | Oxidized glutathione disulfide |
| H2RA | $H_2$ receptor antagonist |
| HA | Hemolytic anemia |
| Hb | Hemoglobin |
| Hct | Hematocrit |
| HCV | Hepatitis C virus |
| Hcy | Homocysteine |

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|---|---|
| HELLP | Hemolysis, elevated liver enzymes, low platelets. |
| Hemoglobin F | Fetal hemoglobin |
| HHV-6 | Human herpesvirus-6 |
| HIT | Heparin-induced thrombocytopenia |
| HIV | Human immunodeficiency virus |
| HLA | Human leukocyte antigens |
| HMW-K | High-molecular-weight kininogen |
| HPA-1 | Human platelet antigen-1 |
| HUS | Hemolytic uremic syndrome |
| ICU | Intensive care unit |
| Ig | Immunoglobulin |
| IGF-I | Insulin like growth factor-I |
| IHA | Immune hemolytic anemia |
| INH | Isoniazid |
| INR | International normalized ratio |
| IS | Immunosuppression |
| ITP | Idiopathic thrombocytopenic purpura |
| IV | Intravenous |
| IVIG | Intravenous Immune Globulin |
| Ka | Kallikrein |
| LA | Lupus anticoagulant |
| LD | Lactate dehydrogenase |

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|---|---|
| LGL | Large granular lymphocyte |
| LMWH | Low molecular-weight heparin |
| MCD | Mean cell diameter |
| MCH | Mean corpuscular hemoglobin |
| MCHC | Mean corpuscular hemoglobin concentration |
| MCV | Mean corpuscular volume |
| MDI | Microbiologically documented infection |
| MDS | Myelodysplastic syndromes |
| MPO | Myeloperoxidase |
| MS | Methionine synthase |
| MTase | Methyltransferase |
| MUD | Matched unrelated donor |
| NADPH | Nicotinamide adenine dinucleotide phosphate |
| NIPA | Non-immune protein adsorption |
| NMTT | N-methyl-thiotetrazole |
| NSAIDs | Nonsteroidal anti-inflammatory drugs |
| PAI-1 | Plasminogen activator inhibitor-1 |
| PCCs | Prothrombin complex concentrates |
| PCI | Percutaneous coronary intervention |
| PF4 | Platelet factor-4 |
| PHSC | The pluripotential hematopoietic stem cell |
| PL | Platelet phospholipid |

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|---|---|
| PMNLs | Polymorph nuclear leukocytes |
| PRCA | Pure red cell aplasia |
| Pre-K | Prekallikrein |
| PT/aPTT | Prothrombin time/activated Partial thromboplastin time |
| PTA | Plasma thromboplastin antecedent |
| PTC | Plasma thromboplastic component |
| PTP | Post transfusion purpura |
| RBCs | Red blood cells |
| rVIIa | Recombinant activated VII |
| SAA | Severe aplastic anemia |
| SAH | S-adenosylhomocysteine |
| SAHH | SAH hydrolase |
| SAM | S-adenyosylmethionine |
| SAs | Sideroblastic anemias |
| SC | Subcutaneous |
| SJS/TEN | Stevens-Johnson syndrome/toxic epidermal necrolysis |
| SLE | Systemic Lupus Erythematosus |
| SSKI | Potassium iodide |
| TCY | Thrombocytopenia |
| THF | Tetrahydrofolate |
| TMAs | Thrombotic microangiopathies |
| TMP/SMX | Trimethoprim/sulfamethoxazole |

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|---|---|
| t-PA | Tissue plasminogen activator |
| TPE | Therapeutic plasma exchange |
| TTP | Thrombotic thrombocytopenic purpura |
| UFH | Unfractionated heparin |
| VIT | Vancomycin induced thrombocytopenia |
| VKA | Vitamin K antagonist therapy |
| VTE | Venous thromboembolism |
| vWF | von Willebrand factor |
| WHO | World Health Organization |

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# Introduction

Blood disorders are a rare, yet extremely serious, adverse effect of drug treatment. Outside of the more predictable bone marrow depression seen with cytotoxic and immunosuppressant agents, drugs in more common use have also been associated with blood disorders ***(Stephens, 2004).***

Although anecdotal reports of drug-induced blood disorders are common in the literature, they often have speculative mechanisms and questionable causality ***(Medina and George, 2001).*** The true incidence of drug-induced blood disorders is therefore difficult to ascertain, but it is clear that they make a major contribution to the incidence of blood disorders ***(Anderson et al., 2004).***

Blood diseases cover a wide spectrum of illnesses ranging from anemia, amongst the most common disorders affecting mankind, to relatively rare conditions such as congenital coagulation disorders. Drugs can induce almost the entire spectrum of hematologic disorders affecting white cells, red cells, platelets and the coagulation system ***(Mintzer et al., 2009).***

The interaction between a drug and red cell membrane produces a composite antigenic structure (or neo antigen), provoking two types of antibodies which mediates drug-induced immune hemolytic anemia ***(Murphy et al., 2009).***

A rare failure of hemopiotic stem cells disorder, aplastic anemia and pure red cell aplasia can be associated with administration of antithyroid drugs as carbimazole or antiepileptic drugs as phenytoin ***(Brodsky and Jones, 2005).***