

Contents

Introduction	10
Pathophysiology of Fibrinogen	12
2.1. Hereditary Fibrinogen Disorders.....	12
2.1.1. Type I Fibrinogen Deficiency.....	12
2.1.2. Type II Fibrinogen Deficiency.....	13
2.1.3. Laboratory Testing and Treatments.....	13
2.2. Genetic Polymorphisms and Altered Fibrin Structure.....	13
2.3. Hyperfibrinogenaemia.....	14
2.4. Disseminated Intravascular Coagulation.....	14
2.5. Fibrinogen Disorders in Major Trauma.....	14
2.6. Fibrinogen Disorders in Cardiovascular Surgery.....	16
2.7. Fibrinogen Disorders in Liver Transplantation.....	17
2.8. Fibrinogen Disorders in Obstetric Haemorrhage.....	18
2.9. Summary and Perspectives.....	18
2.10. References.....	19
Fibrinogen in Cardiac Surgery	24
3.1. Mechanisms of Fibrinogen Consumption during Cardiac Surgery.....	24
3.2. The Association between Bleeding and Fibrinogen Levels.....	25
3.3. Fibrinogen Supplementation in Cardiac Surgery.....	27
3.4. Paediatric Setting.....	30
3.5. Conclusion.....	30
3.6. References.....	31
Fibrinogen and Other Factor Concentrates in Trauma Bleeding	33
4.1. Mechanism of Bleeding in Trauma – Setting the Scene.....	33
4.2. Monitoring – or Why are Viscoelastic Tests Important.....	34
4.3. Fibrinogen Concentrate – How and Why.....	35
4.4. Timing for Fibrinogen – Sequence of Actions.....	38
4.5. Is there an Indication for Prothrombin Complex Concentrate (PCC) in Trauma?.....	38
4.6. PCC, New Oral Anticoagulant Agents (NOACs) and Trauma.....	39
4.7. One Patient – More Than One Concentrated Factor: Both Fibrinogen and PCC.....	40
4.8. Conclusion.....	41
4.9. References.....	41
Fibrinogen and Peri-Partum Haemorrhage	45
5.1. Hypofibrinogenaemia is a Risk Marker of PPH Severity.....	46
5.2. The Way to Correct Fibrinogen Plasma Level.....	47
5.3. When Should Hypofibrinogenaemia Be Corrected?.....	50
5.4. Which Fibrinogen Concentrate Dose Target to Stop Bleeding?.....	51
5.5. Is Concomitant Inhibition of Fibrinolysis Indicated?.....	51
5.6. When do We Need Drugs to Boost Thrombin Generation?.....	52
5.7. Factor XIII in PPH Induced Coagulopathy.....	52
5.8. Balanced Benefit Risk Regarding Side Effects and Economic Balance.....	54

5.9.	Who Should Correct Hypofibrinogenaemia?	54
5.10.	Conclusion	54
5.11.	References.....	54

Fibrinogen and Other Concentrates in Paediatric Patients 57

6.1.	Fibrinogen Physiologic and Pathological Role in Haemostasis	57
6.2.	Fibrinogen Supplementation Modalities.....	58
6.3.	Fibrinogen Concentrate.....	58
6.4.	Prothrombin Complex Concentrate	59
6.5.	Factor XIII Concentrate.....	60
6.6.	Recombinant Activated Factor VII	60
6.7.	Antifibrinolytics.....	60
6.8.	References.....	61

Fibrinogen Replacement: Plasma, Cryoprecipitate, Concentrate 64

7.1.	Available Sources for Fibrinogen Supplementation	64
7.2.	Use and Comparison of Plasma and Fibrinogen Concentrate	65
7.3.	Further Research, Experimental Studies and Outlook of Fibrinogen Supplementation	66
7.4.	Conclusion	66
7.5.	References.....	66

Factor Concentrates (Fibrinogen, PCC, FXIII) versus Cryoprecipitate 70

8.1.	Cryoprecipitate	70
8.2.	Prothrombin Complex Concentrates	72
8.3.	Factor XIII.....	73
8.4.	Fibrinogen Concentrate.....	73
8.5.	Conclusion	74
8.6.	References.....	74

Factor Concentrates (Fibrinogen, PCC, FXIII) versus FFP in Patient Blood Management 77

9.1.	Fresh Frozen Plasma	77
9.2.	Fibrinogen.....	80
9.3.	Prothrombin Complex Concentrate	82
9.4.	FXIII	83
9.5.	Conclusion	85
9.6.	References.....	85

Fibrinogen in the ESA Guidelines 91

10.1.	An Introduction to the GRADE System	91
10.2.	Fibrinogen Recommendations of the ESA Guideline 2017	94
10.3.	Randomized Controlled Trials Evaluating Fibrinogen Concentrate	94
10.4.	Bias Assessment of Randomized Controlled Trials	94
10.5.	Bias related to observational, non-randomized studies	99
10.6.	Conclusion	101
10.7.	References	101

Index 103