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中文翻译版
原书第2版

哈里森 血液学与肿瘤学

Harrison's Hematology and Oncology

原著 Dan L. Longo
主译 薛妍 陈衍



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内 容 简 介

本书是世界著名的哈里森系列教科书之一,是在第18版《哈里森内科学》基础上编撰而成。分为12部分,共55章,分别介绍了造血的细胞基础、血液系统疾病的主要临床表现、贫血、骨髓增殖性疾病、血液肿瘤、止血障碍、肿瘤生物学、癌症预防和治疗原则、肿瘤性疾病、内分泌肿瘤、癌症的间接影响、肿瘤相关急症和晚期并发症的影响。本书系统回顾了血液系统常见疾病和多种恶性实体肿瘤的流行病学、病因、临床表现、诊断、分期、治疗和预防相关内容。另外,还有关于血液学和肿瘤学相关的基础知识,如血细胞生成、癌细胞生物学、癌症预防的独立篇章,内容囊括了这些领域的前沿发展。

本书是血液学和肿瘤学临床医生、科研人员、医学院校研究生的必备参考书,还适用于开展内科系统的医学继续教育工作。

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HARRISON'STM

HEMATOLOGY AND ONCOLOGY

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译者前言

《哈里森血液学与肿瘤学》是世界著名的哈里森系列教科书之一,权威性高、实用性强,本书是在第18版《哈里森内科学》基础上编撰而成。

本书分为12部分,共55章,分别介绍了造血的细胞基础、血液系统疾病的主要临床表现、贫血、骨髓增殖性疾病、血液肿瘤、止血障碍、肿瘤生物学、癌症预防和治疗原则、肿瘤性疾病、内分泌肿瘤、癌症的间接影响、肿瘤相关急症和晚期并发症的影响。本书系统回顾了血液系统常见疾病和多种恶性实体肿瘤的流行病学、病因、临床表现、诊断、分期、治疗和预防相关内容。另外,还设独立篇章介绍了血细胞生成、癌细胞生物学、癌症预防等领域的前沿进展。

本书是血液学和肿瘤学临床医生、科研人员、医学院校研究生的必备参考书,也可用于内科系统的医学继续教育。翻译人员具有多年的临床工作经验和科研经历。在此,衷心感谢各位译者的倾情付出和大力支持。

因译者能力有限,书中可能存在不当和疏漏之处,敬请读者不吝指教。

第四军医大学西京医院 薛 妍 陈 衍

2018年1月

《哈里森内科学》在血液学领域享誉悠久。Maxwell Wintrobe 是血液学杰出专家,他的工作为血液学成为内科学亚专业奠定了基础。作为最先参与此项工作的编辑,Maxwell Wintrobe 参与了前 7 版《哈里森内科学》的出版,在第 6 版和第 7 版中作为主编替代了 Tinsley Harrison。Wintrobe 生于 1901 年,1927 年作为新奥尔良杜兰大学的一名医学助理开始深入研究血液疾病。1930—1943 年,他在约翰·霍普金斯大学继续研究。1943 年,转到犹他大学继续工作,直至 1986 年去世。现在临床常规用于描述红细胞异常的很多参数是由 Wintrobe 创造的,包括血细胞比容、红细胞指数和红细胞沉降率,他还给这些参数定义了正常值和异常值。在他 50 年的研究生涯中,还有很多其他重要的贡献。

作为一门医学亚专业学科,肿瘤学发展较晚,它是作为血液学的特殊亚学科发展起来的。在 20 世纪 50 年代中期到 60 年代初期,一些对血液肿瘤有着特殊兴趣的血液学家,开始应用化学药物治疗白血病和淋巴瘤。随着新型药物和临床研究的研发与进展,肿瘤学知识体系不断发展壮大,开始独立于血液学。一方面,基于肿瘤生物学的研究,人们对血液肿瘤的关注扩展到全身各系统肿瘤;另一方面,随着人们对凝血相关疾病认识的深入,这类疾病也占据了血液疾病的很大部分;这两方面原因加速了肿瘤学与血液学的分离,使肿瘤学成为一门独立学科。

现在,尽管很多医学研究中心的血液学和肿瘤学仍合并在一起,但已经在概念上明确区分开来。血液学和肿瘤学具有各自独立的奖学金培训项目(尽管还有很多联合培养项目)、独立的学会认证考试、独立的专业组织、独立的教科书和独立的知识体系,这使得两者差别更为明显。在一些医学研究中心,肿瘤学不再仅是内科学的一个亚专业,而是一个完全独立的学科,地位与内科相当。经济因素也促进血液学和肿瘤学的分离。

也许上述观点存有偏见,但我的确不赞成将医学亚专业不断细分。现在心脏病专家分有创性和无创性的,胃肠病专家分应用内镜和不应用内镜的,专注于器官的亚专业专家(糖尿病专家、甲状腺专家)也代替了专注于器官系统的亚专业专家(内分泌专家)。当需要快速掌握专业知识时,培训时间却并未延长来适应需求,就很难达到精湛技艺。因此,一定要特别关注实习生的培训时间和培训质量。

尽管现代医学分科越来越精细,学生、实习生、普通内科医生、家庭内科医生、内科医生助教、护理师和非医学专业人士仍需要系统学习血液学和肿瘤学相关知识,帮助他们治疗临床患者。鉴于缺乏血液学和肿瘤学系统知识的学习书籍,《哈里森内科学》的编辑们将血液学和肿瘤学的相关篇章整合起来,编辑成这本《哈里森血液学与肿瘤学》。2010 年根据第 17 版《哈里森内科学》出版了第 1 版《哈里森血液学与肿瘤学》,由于反响良好,在第 18 版《哈里森内科学》基础上又出版了第 2 版《哈里森血液学与肿瘤学》。

本书包括 12 部分共 55 章,这 12 部分是:①造血的细胞基础;②血液系统疾病的主要临床表现;③贫血;④骨髓增殖性疾病;⑤血液肿瘤;⑥止血障碍;⑦肿瘤生物学;⑧癌症预防和治疗的原则;⑨肿瘤性

疾病;⑩内分泌肿瘤;⑪癌症的间接影响;⑫肿瘤相关急症和晚期并发症的影响。

每一篇章都是由在相关领域具有开创性贡献的专家撰写,内容具有权威性和先进性。每一篇章包含遗传学、细胞生物学、病理生理学和疾病治疗等内容。另外,关于血细胞生成、癌细胞生物学、癌症预防的独立篇章囊括了这些领域的最新进展,也是血液学和肿瘤学相关疾病的基础。

将血液学和肿瘤学合并在一本书内并不常见,我们希望这样会对读者有用。像医学的许多领域一样,血液学和肿瘤学知识体系也在飞速进展着。改变临床实践的新发现不断涌现,这需要付出持之以恒的努力才能同步跟随。我们希望这本书能对您的临床工作有所帮助。

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Dan L. Longo MD

CONTENTS

目 录

第一部分 造血的细胞基础

第 1 章 造血干细胞	3
David T. Scadden Dan L. Longo	

第二部分 血液系统疾病的主要临床表现

第 2 章 贫血及红细胞增多症	11
John W. Adamson Dan L. Longo	
第 3 章 出血和血栓形成	22
Barbara Konkle	
第 4 章 淋巴结肿大和脾大	31
Patrick H. Henry Dan L. Longo	
第 5 章 粒细胞及单核细胞疾病	39
Steven M. Holland John I. Gallin	
第 6 章 血液学总论和外周血涂片分析	54
Dan L. Longo	

第三部分 贫 血

第 7 章 铁缺乏及其他造血障碍性贫血	69
John W. Adamson	
第 8 章 血红蛋白异常性疾病	78
Edward J. Benz, Jr	
第 9 章 巨幼细胞贫血	90
A. Victor Hoffbrand	
第 10 章 溶血性贫血和急性失血性贫血	102
Lucio Luzzatto	
第 11 章 再生障碍性贫血、骨髓增生异常综合征及相关骨髓衰竭综合征	118
Neal S. Young	
第 12 章 输血生物学与治疗	131
Jeffery S. Dzieczkowski Kenneth C. Anderson	

第四部分 骨髓增殖性疾病

第 13 章	真性红细胞增多症和其他骨髓增殖性疾病	141
	Jerry L. Spivak	

第五部分 血液肿瘤

第 14 章	急性和慢性髓细胞白血病	153
	Meir Wetzler Guido Marcucci Clara D. Bloomfield	
第 15 章	淋巴细胞恶性肿瘤	170
	Dan L. Longo	
第 16 章	不常见的血液系统恶性肿瘤	190
	Dan L. Longo	
第 17 章	浆细胞疾病	198
	Nikhil C. Munshi Dan L. Longo Kenneth C. Anderson	
第 18 章	淀粉样变性	209
	David C. Seldin Martha Skinner	

第六部分 止血障碍

第 19 章	血小板和血管壁疾病	219
	Barbara Konkle	
第 20 章	凝血功能障碍	229
	Valder R. Arruda Katherine A. High	
第 21 章	动脉和静脉血栓形成	240
	Jane E. Freedman Joseph Loscalzo	
第 22 章	肺血栓栓塞	246
	Samuel Z. Goldhaber	
第 23 章	抗血小板抗凝和纤维溶解药物	255
	Jeffrey I. Weitz	

第七部分 肿瘤生物学

第 24 章	肿瘤遗传学	277
	Pat J. Morin Jeffrey M. Trent Francis S. Collins Bert Vogelstein	
第 25 章	癌症细胞生物学和血管生成	288
	Dan L. Longo	

第八部分 癌症预防和治疗的原则

第 26 章	癌症治疗策略	311
	Dan L. Longo	

第 27 章	肿瘤的预防和早期检测	322
	Jennifer M. Croswell Otis W. Brawley Barnett S. Kramer	
第 28 章	肿瘤治疗原则	333
	Edward A. Sausville Dan L. Longo	
第 29 章	肿瘤相关感染	361
	Robert Finberg	
第 30 章	造血细胞移植	373
	Frederick R. Appelbaum	
第 31 章	妊娠期肿瘤	382
	Dan L. Longo	
第 32 章	姑息治疗和临终关怀	386
	Ezekiel J. Emanuel	

第九部 肿瘤性疾病

第 33 章	皮肤癌	409
	Walter J. Urbani Carl V. Washington Hari Nadiminti	
第 34 章	头颈部癌	421
	Everett E. Vokes	
第 35 章	肺部肿瘤	426
	Leora Horn William Pao David H. Johnson	
第 36 章	胸腺瘤	445
	Dan L. Longo	
第 37 章	乳腺癌	448
	Marc E. Lippman	
第 38 章	胃肠道癌	459
	Robert J. Mayer	
第 39 章	肝胆管肿瘤	472
	Brian L. Carr	
第 40 章	胰腺癌	482
	Irene Chong David Cunningham	
第 41 章	膀胱癌和肾细胞癌	487
	Howard I. Scher Robert J. Motzer	
第 42 章	前列腺良、恶性疾病	494
	Howard I. Scher	
第 43 章	睾丸癌	505
	Robert J. Motzer George J. Bosl	
第 44 章	妇科恶性肿瘤	511
	Michael V. Seiden	
第 45 章	软组织肉瘤、骨肉瘤、骨转移癌	518
	Shreyaskumar R. Patel Robert S. Benjamin	
第 46 章	原发和转移性神经系统肿瘤	524
	Lisa M. DeAngelis Patrick Y. Wen	

第 47 章	原发灶不明癌	538
	Gauri R. Varadhachary James L. Abbruzzese	

第十部分 内分泌肿瘤

第 48 章	甲状腺癌	545
	J. Larry Jameson Anthony P. Weetman	
第 49 章	胃肠胰腺神经内分泌肿瘤	553
	Robert T. Jensen	
第 50 章	多发性内分泌肿瘤	572
	Camilo Jimenez Vasquez Robert F. Gagel	
第 51 章	嗜铬细胞瘤和肾上腺皮质癌	580
	Hartmut P. H. Neumann Wiebke Arlt Dan L. Longo	

第十一部分 癌症的间接影响

第 52 章	副肿瘤综合征:内分泌与血液系统	593
	J. Larry Jameson Dan L. Longo	
第 53 章	副肿瘤神经综合征	601
	Josep Dalmau Myrna R. Rosenfeld	

第十二部分 肿瘤相关急症和晚期并发症的影响

第 54 章	肿瘤相关急症	611
	Rasim Gucalp Janice Dutcher	
第 55 章	癌症及其治疗的后期影响	626
	Carl E. Freter Dan L. Longo	
彩图		633

第一部分 造血的细胞基础

第 1 章

Chapter 1

造血干细胞

David T. Scadden Dan L. Longo

外周血中所有类型的细胞及全身各组织中的一些细胞均来源于造血干细胞。如果造血干细胞受损失去功能(如核事故所致),在缺乏额外支持治疗时,人体只能存活 2~4 周。随着造血干细胞的临床应用,每年有数以千百万的生命得以拯救(详见第 30 章)。约几十万的干细胞池中可产生数百亿的造血细胞。造血干细胞如何造血,在历经数十年的时间里如何满足造血需求,在临床中如何才能充分使用造血干细胞是医学面临的主要问题。

研究血细胞的产生过程,也为其他组织产生及受到调控的可能过程给予了有力的提示。造血的基础研究,包括确定细胞在功能性成熟的改变过程中所伴随的分子改变、分类细胞为不同的功能性亚组,阐述特定微环境对造血干细胞的调控作用,也为其他组织的发育提供模型。而且这些概念不仅局限于正常组织,还可延伸到组织的恶性变。干细胞在异质性的细胞群中数量很少,其生物学功能仅在一些涉及造血重组研究的动物模型中被观察研究。因此,我们对干细胞的了解主要基于一些基因调控的动物模型的结果。

造血干细胞的主要功能

所有的干细胞具有两个主要功能:自我更新及分化(图 1-1)。造血干细胞主要用于生成、维持及修复组织。在长期的生命过程中,干细胞成功地补充了生存期较短的成熟细胞。这种自我更新的过程可确保干细胞能够维系其数量。没有自我更新,干细胞池会出现枯竭,而且也不可能维系组织的形成。分化的过程也引起组织功能的产生:生成成熟细胞。没有正确的分化,组织功能的完整性将会受损,器官功能也会受损。

在外周血中,成熟细胞的平均寿命不同,成熟

中性粒细胞为 7h,红细胞为数月,记忆淋巴细胞为数年。但是,干细胞池是所有血细胞及免疫细胞的中心及永久来源,具有通过单细胞来源产生大量细胞群的功能,而且在数十年里保持旺盛生命力。作为单个干细胞,具有以下三种功能:生成两个干细胞;生成两个具有不同分化能力的细胞;生成一个干细胞及另一个分化的细胞。前两种是干细胞对称分裂的结果,后一种则是干细胞分化为不同子细胞的结果——通过不对称分裂。在机体发育过程中,或特定状态下,干细胞的这些不同分化方式处于动态的变化和平衡中。

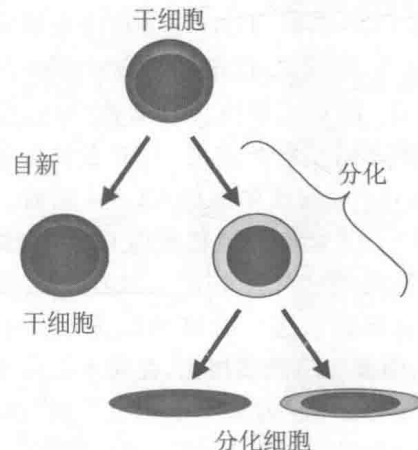


图 1-1 干细胞的特征

干细胞有两个基本特征:分化成各种成熟细胞的能力和自我更新的能力。与自我更新相关的内源性因子包括 Bmi 1、Gfi 1、PTEN、STAT5、Tel/Atv6、p21、p18、MCL-1、Mel-18、RAE28 和 HoxB4 的表达。外源性自我更新的信号包括 Notch、Wnt、SHH 和 tie-2/Ang-1。基于小鼠研究,造血干细胞主要表达以下细胞表面分子:CD34、Thy 1 (CD90)、c-kit 受体 (CD117)、CD133、CD164 和 c-Mpl (CD110 也被称为血小板生成素受体)