·指南与共识·

编者按　严重过敏反应是指机体在接触过敏原后突发的、严重的、可危及生命的全身性过敏反应，诊断不及时、救治不当可导致严重后果。《严重过敏反应急救指南》是在国家卫生健康委员会医疗管理服务指导中心的指导下，由多个相关学会和机构合作制订的循证指南。在该指南全文正式发布前，本刊先行刊出该指南关于严重过敏反应诊断、救治和救治后管理的 26 条推荐意见，以使临床尽快得到关于严重过敏反应急救的指导，同时征求对该指南的反馈意见。

《严重过敏反应急救指南》推荐意见

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【摘要】《严重过敏反应急救指南》的推荐意见围绕严重过敏反应的诊断、救治准备、救治措施和救治后管理回答了 15 个临床问题，共形成 26 条推荐意见。推荐意见中的证据质量分为高、中、低和极低 4 级，推荐强度分为强、弱 2 级。推荐意见的强度主要基于对利弊的权衡，不完全依赖于证据质量。临床严重过敏反应的急救可参照推荐意见实施。

【关键词】 指南；　过敏反应；　休克；　急救医学；　循证医学；　肾上腺素；　糖皮质激素类

Recommendations in *Guideline for Emergency Management of Anaphylaxis*

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【Abstract】 The recommendations of *Guideline for Emergency Management of Anaphylaxis* answered 15 clinical questions about diagnosis, preparation for treatment, treatment measures, and post-treatment management of anaphylaxis and a total of 26 recommendations were formed. In the recommendations, the quality of evidence was divided into 4 levels: high, moderate, low, and very low. And the strength of recommendation was divided into 2 levels: strong and weak. The strength of recommendations was mainly determined by weighing the advantages and disadvantages, instead of relying on the quality of evidence. Emergency management of anaphylaxis in clinical practice could be carried out with reference to the recommendations of this guideline.

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【Key words】 Guideline; Anaphylaxis; Shock; Emergency medicine; Evidence-based medicine; Epinephrine; Glucocorticoids

严重过敏反应是指机体在接触过敏原后突发的、严重的、可危及生命的全身性过敏反应[1]。其主要临床特征为快速出现威胁生命的呼吸系统或/和循环系统问题,大部分情况下会出现皮肤黏膜系统症状[2]。严重过敏反应通常在患者接触过敏原后数分钟至数小时内发作[1]。部分患者(0.4% ~23.3%)会发生双相反应,即患者初次发作的症状缓解后,在未接触过敏原的情况下严重过敏反应的症状再次发作[3-5];双相反应的发作间隔时间范围为数分钟至数天[4]。还有小部分患者会发生迟发性严重过敏反应,即在接触过敏原后数小时至数天内发作[6-8]。

我国对严重过敏反应的认识尚存在不足,缺少统一的诊断标准和救治规范,临床救治措施有许多不合理之处[9-10],亟需科学、合理的指导。因此,在国家卫生健康委员会医疗管理服务指导中心的指导下,由中国药理学会药源性疾病学专业委员会、中国医师协会变态反应医师分会、中华医学会变态反应学分会、中华医学会急诊医学分会、中华医学会呼吸病学分会、中华医学会麻醉医学分会、中国药学会医院药学专业委员会和中华护理学会联合发起《严重过敏反应急救指南》制订,由北京大学第三医院药剂科负责进行相关调研、制作循证证据并起草指南,兰州大学循证医学中心提供技术支持。根据美国医学科学院制定的临床实践指南定义[11]和 2014 年发布的《世界卫生组织指南制订手册》中关于指南的制订流程以及相关方法学标准[12],指南的制订流程包括指南项目组筹建、指南注册与撰写计划书、临床问题和结局指标的收集与遴选、开题会确定临床问题与结局指标排序、证据的制作与形成、推荐意见的起草、专家共识形成推荐意见、推荐意见的外审与修订、指南全文的撰写与发布、指南的传播与实施、指南的评价及更新等。

本指南采用推荐分级的评估、制定与评价标准(Grades of Recommendations Assessment, Development and Evaluation,GRADE)系统评价原始证据,将证据质量分为高(A)、中(B)、低(C)和极低(D)4 级,将推荐强度分为强(1)、弱(2)2 级(表 1)[13-14]。在使用指南研究与评价工具(Appraisal of Guidelines for Research and Evaluation, AGREE Ⅱ)[15]评价其他指南[2-3, 16-32]的基础上,本指南项目组专家基于现有最佳证据与经验形成推荐意见;推荐意见的强度主要基于对利弊的权衡,不完全依赖于证据质量[13]。

完整的指南包括前言、制订方法与正文 3 部分,正文包括推荐意见、证据总结、推荐说明等内容。推荐意见部分由围绕严重过敏反应的诊断、救治准备、救治措施和救治后管理等方面的 26 条推荐意见组成。现先行发表该指南的 26 条推荐意见,全文及相关资料以后将在其他刊物上发表。

1　严重过敏反应的诊断

临床问题 1　诊断标准是什么?

推荐意见　严重过敏反应的诊断应采用表 2 列出的诊断标准,并注意患者可能出现其他非典型的症状。(1A,强推荐,高质量证据[33-34])

临床问题 2　严重过敏反应如何分级?

推荐意见　严重过敏反应分级标准见表 3,以患者出现的最严重症状为准。(1D,强推荐,极低质量证据)

表 1　推荐分级的评估、制定与评价标准中关于证据质量等级与推荐强度的描述

Tab 1　Description about quality of evidence and strength of recommendations in Grades of Recommendations Assessment, Development and Evaluation

分级	具体描述	研究类型
证据质量		
高质量(A)	非常确信真实的效应值接近效应估计值	1. 设计优良的随机对照试验 2. 质量升高 2 级的观察性研究
中等质量(B)	对估计效应值有中等程度的信心:真实效应值可能与估计效应值相近,不排除大不相同的可能	1. 质量降低 1 级的随机对照试验 2. 质量升高 1 级的观察性研究
低质量(C)	对估计效应值的信任程度有限:真实效应值可能与估计效应值大不相同	1. 质量降低 2 级的随机对照试验 2. 观察性研究
极低质量(D)	对估计效应值几乎没有信心,真实效应值很可能与估计效应值大不相同	1. 质量降低 3 级的随机对照试验 2. 质量降低 1 级的观察性研究 3. 病例序列报告 4. 个案报道
推荐强度		
强(1)	遵从推荐意见利大于弊	
弱(2)	遵从推荐意见时利弊不确定或利弊相当(证据质量、意愿和价值观等方面可能存在较大不确定性)	

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表 2　严重过敏反应的诊断标准[a]

Tab 2　Diagnostic criteria for anaphylaxis

当症状满足以下 3 个标准的任意一个时,患者极可能发生了急性严重过敏反应	
1	疾病呈急性发作(几分钟至数小时内),有皮肤和/或黏膜系统症状,如皮疹,瘙痒或潮红,唇舌红肿和/或麻木等,及以下任一系统症状(不考虑过敏原接触史) A. 呼吸系统症状,如音哑、咳嗽、胸闷、气短、呼吸困难、喘鸣、支气管痉挛、发绀、呼气流量峰值下降、血氧不足等 B. 血压下降(见标准 3)或其相关的终末器官功能障碍,如麻木、肌张力减退、晕厥、大小便失禁等
2	患者接触可疑过敏原后几分钟至数小时内有下述 2 项及以上的症状快速发作 A. 皮肤黏膜组织症状,如各种皮疹,瘙痒或潮红,唇舌红肿和/或麻木等 B. 呼吸系统症状,如胸闷、气短、呼吸困难,喘鸣,支气管痉挛,发绀,呼气流量峰值下降,血氧不足等 C. 血压下降或终末器官功能受累,如肌张力减退,晕厥,大小便失禁等 D. 持续的胃肠系统症状,如腹痛、恶心、呕吐等
3	患者接触已知过敏原后几分钟至数小时内血压下降 A. 婴儿与儿童:收缩压低于相应年龄的正常值[<1 岁,收缩压 <70 mmHg;1 ~10 岁,收缩压 <(70 mmHg + 2 × 年龄);11 ~17 岁,收缩压 <90 mmHg] 或比基础值下降 >30% B. 成人:收缩压低于 90 mmHg 或比基础值下降 >30%

注　[a]:基于美国国立变态反应和传染病研究所/食物过敏和过敏反应网络的诊断标准[1],并参考我国医务工作者临床经验改编;1 mmHg = 0.133 kPa

表 3　严重过敏反应的分级标准[a]

Tab 3　Grading criteria for anaphylaxis

分级	临床表现
Ⅰ级	只有皮肤黏膜系统症状和胃肠系统症状,血流动力学稳定,呼吸系统功能稳定 皮肤黏膜系统症状:皮疹,瘙痒或潮红,唇舌红肿和/或麻木等 胃肠系统症状:腹痛,恶心、呕吐等
Ⅱ级	出现明显呼吸系统症状或血压下降 呼吸系统症状:胸闷、气短、呼吸困难、喘鸣、支气管痉挛、发绀、呼气流量峰值下降、血氧不足等 血压下降:成人收缩压 80 ~90 mmHg 或比基础值下降 30% ~40%;婴儿与儿童:<1 岁,收缩压 <70 mmHg;1 ~10 岁:收缩压 <(70 mmHg +2 × 年龄);11 ~17 岁:收缩压 <90 mmHg 或比基础值下降 30% ~40%
Ⅲ级	出现以下任一症状:神志不清、嗜睡、意识丧失、严重的支气管痉挛和/或喉头水肿、发绀、重度血压下降(收缩压 <80 mm Hg 或比基础值下降 >40%)、大小便失禁等
Ⅳ级	发生心跳和/或呼吸骤停

注　[a]:参考 Brown[35] 提出的标准;1 mmHg = 0.133 kPa

2　严重过敏反应救治的准备

临床问题 3　在医务工作者到来之前,患者/旁人应当采取何种措施?

推荐意见　患者发生疑似严重过敏反应后,患者/旁人应立即拨打急救电话或送往附近医院,并应当寻求在场或附近的医务工作者帮助。在医务工作者到来前,应尽可能迅速地使患者脱离过敏原,平卧;如果患者有呕吐,应保持患者头部偏向一侧并清除异物,以防患者误吸呕吐物导致窒息。(1D,强推荐,极低质量证据[36])

临床问题 4　对院前和院内的急救设备有何要求?

推荐意见　院前和院内的急救设备中应当配备肾上腺素注射液,根据相关规定及资源的可及性进行其他配备。(1D,强推荐,极低质量证据[36-37])

3　严重过敏反应的救治措施

临床问题 5　严重过敏反应救治过程中应当如何进行监护?

推荐意见　严重过敏反应救治过程中应对心脏、血压、呼吸、血氧饱和度实施密切监护。(1D,强推荐,极低质量证据)

临床问题 6　何种情况下需要建立人工气道,以及如何实施?

推荐意见　对于严重过敏反应患者,当发生气道水肿或支气管痉挛而导致严重呼吸困难时,应考虑气管插管或气管切开,紧急情况下对成人可行环甲膜穿刺。(1D,强推荐,极低质量证据)

临床问题 7　救治中应当如何正确使用肾上腺素?

临床问题 7.1　肾上腺素在严重过敏反应救治中的地位是什么?

推荐意见　对于Ⅱ级及以上的严重过敏反应患者,肾上腺素是救治的首选药物。(1B,强推荐,中等质量证据[36-52])

临床问题 7.2　肾上腺素的使用时机是什么?

推荐意见　肾上腺素应在患者被确诊为Ⅱ级及以上的严重过敏反应后尽早使用。(1C,强推荐,低质量证据[38-39])

临床问题 7.3　何种情况下,肾上腺素的给药方式应该采用肌内注射?

推荐意见　对于Ⅱ、Ⅲ级反应患者,应首选肌内注射肾上腺素;对于胃肠系统症状难以缓解的Ⅰ级反应患者也可考虑肌内注射肾上腺素。(1C,强推荐,低质量证据[53-58])

临床问题 7.4　肌内注射肾上腺素时应如何选择剂量和浓度?

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推荐意见　剂量：肾上腺素按 0.01 mg/kg 体重给予，14 岁及以上患者单次最大剂量不超过 0.5 mg，14 岁以下患者单次最大剂量不超过 0.3 mg；浓度：1 mg/ml（1∶1 000），等同于 1 ml∶1 mg 规格的肾上腺素注射液浓度；5～15 min 后效果不理想者可重复给药。（1D，强推荐，极低质量证据[37]）

临床问题 7.5　肌内注射肾上腺素应该在什么部位？

推荐意见　肌内注射肾上腺素的部位为大腿中部外侧。（1C，强推荐，低质量证据[37, 54]）

临床问题 7.6　何种情况下，肾上腺素应该采用静脉注射方式给药？

推荐意见　对于已发生或即将发生心跳和/或呼吸骤停的Ⅳ级反应患者，应静脉注射肾上腺素；对发生Ⅲ级反应且在 ICU 内/手术期间已建立静脉通路并得到监护的患者，可静脉注射肾上腺素。（1C，强推荐，低质量证据[57-58]）

临床问题 7.7　静脉注射肾上腺素应如何选择剂量和浓度？

推荐意见　静脉注射肾上腺素单次剂量，Ⅲ级反应：14 岁以上儿童及成人 0.1～0.2 mg，≤14 岁儿童 2～10 μg/kg；Ⅳ级：14 岁以上儿童及成人 0.5～1 mg，≤14 岁儿童 0.01～0.02 mg/kg；浓度：0.1 mg/ml（1∶10 000），即将现有 1 ml∶1 mg 规格的肾上腺素注射液稀释 10 倍；3～5 min 后效果不理想者可重复给药。（2D，弱推荐，极低质量证据）

临床问题 7.8　何种情况下，肾上腺素应该采用静脉滴注方式给药？

推荐意见　对于Ⅱ、Ⅲ级反应患者，静脉注射/肌内注射肾上腺素 2～3 次后，或 ICU 内/手术期间已建立静脉通路并得到监护后，可静脉滴注肾上腺素；对于Ⅳ级反应患者，症状改善但未完全缓解时，可考虑静脉滴注肾上腺素。（2C，弱推荐，低质量证据[36, 57-58]）

临床问题 7.9　静脉滴注肾上腺素应如何选择剂量和浓度？

推荐意见　静脉滴注肾上腺素的剂量为 3～20 μg/（kg·h）；浓度为 0.1～0.004 mg/ml（1∶10 000～1∶250 000），即将现有 1 ml∶1 mg 规格的肾上腺素注射液稀释 10～250 倍。（2D，弱推荐，极低质量证据）

临床问题 7.10　何种情况下，推荐肾上腺素采用皮下注射方式给药？

推荐意见　不推荐在严重过敏反应的紧急救治中皮下注射肾上腺素。（1C，强推荐，低质量证据[54-55, 59-60]）

临床问题 7.11　使用肾上腺素的禁忌证是什么？

推荐意见　在危及生命的严重过敏反应紧急救治中，肾上腺素的使用没有绝对的禁忌证；但对于有心血管疾病史的患者和老年患者应权衡利弊谨慎使用。（2D，弱推荐，极低质量证据[37]）

临床问题 7.12　如何防范或处理使用肾上腺素所产生的不良反应？

推荐意见　为防范使用肾上腺素所产生的不良反应，应尽量避免不必要的静脉给药；静脉使用肾上腺素时应注意控制浓度，并进行持续心脏、血压、呼吸、血氧饱和度的监测。发生肾上腺素局部不良反应时，可使用酚妥拉明进行局部浸润注射。（1C，强推荐，低质量证据[61-62]）

临床问题 8　H_1 受体拮抗剂在严重过敏反应救治中的地位是什么？

推荐意见　H_1 受体拮抗剂可作为严重过敏反应救治的二线用药，主要用于缓解皮肤黏膜症状，不作为抢救药物使用。Ⅰ级反应患者可予口服，Ⅱ级反应及以上患者在给予肾上腺素抢救后可予口服或静脉滴注。（1D，强推荐，极低质量证据[42-45,48-52,63]）

临床问题 9　吸入 β_2 受体激动剂在严重过敏反应救治中的地位是什么？

推荐意见　短效 β_2 受体激动剂可作为严重过敏反应救治的二线用药，有支气管痉挛、呼吸困难、喘鸣的患者可吸入短效 β_2 受体激动剂。（1D，强推荐，极低质量证据[42-43, 45,47-52, 63]）

临床问题 10　糖皮质激素在严重过敏反应救治中的地位是什么？

推荐意见　糖皮质激素可作为严重过敏反应救治的二线用药。口服或静脉注射糖皮质激素可能会降低发生双相反应或迟发相反应的风险；若患者出现持续的支气管痉挛，可考虑雾化吸入或静脉给予糖皮质激素。（1C，强推荐，低质量证据[36-37,42-52,63-69]）

临床问题 11　液体复苏在严重过敏反应救治中的地位是什么？

推荐意见　液体复苏可用于严重过敏反应伴循环系统不稳定的患者，液体用量一般为 20 ml/kg，根据患者情况调整剂量。（1D，强推荐，极低质量证据[36-37]）

4　严重过敏反应救治后的管理

临床问题 12　救治成功后应当监护多长时间？

推荐意见　严重过敏反应患者经救治脱离危险后，应当在医院监护至少 12 h，监测患者的心脏、血压、呼吸、血氧饱和度和尿量。（1C，强推荐，低质量证据[70]）

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临床问题 13　如何上报药源性严重过敏反应病例?

推荐意见　应上报所有药源性严重过敏反应病例,上报内容包括可疑致敏原、发作症状描述(包括接触致敏原到发作的间隔时间)、抢救措施与患者转归,具体参见《药品不良反应报告和监测管理办法》[71]。(1D,强推荐,极低质量证据)

临床问题 14　患者离院时医护人员应当如何进行患者教育?

推荐意见　患者离院时,医护人员应对患者或患儿的监护人进行疾病定义、诊断标准、避免再次接触潜在过敏原、一线救治措施的宣教,以使患者能够自我识别过敏反应并进行紧急处理。(1C,强推荐,低质量证据[72-73])

临床问题 15　如何预防严重过敏反应的发生?

推荐意见　首选预防措施为避免接触过敏原。既往发生严重过敏反应者必须接触可疑过敏原时,可考虑提前 6 ~ 12 h 应用糖皮质激素进行预防,糖皮质激素可能降低严重过敏反应的发生率,但不能绝对避免严重过敏反应的发生,因而仍需在预防用药后密切监测,做好救治准备。不推荐对无过敏史人群进行预防用药。(1C,强推荐,低质量证据[74-84])

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