Operative Techniques and Recent Advances in Acute Care and Emergency Surgery

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“Ancora imparo” I’m still learning.
(Michelangelo at 87)

Foreword

Across the globe, trauma systems and approaches to the care of critically injured patients vary widely. The emerging paradigm of "acute care surgery" has provided grounds for discussion and debate in the surgical community. First, there appears to exist some confusion related to the underlying terminology. In essence, acute care surgery is defined as a service line that encompasses trauma surgery, emergency general surgery, and surgical critical care. Based on this pragmatic definition, many US surgeons argue that their European colleagues do *not* truly practice acute care surgery, as the component of surgical critical care has been largely outsourced to intensivists and anesthesiologists in European institutions. There is also an argument that many trauma centers in the United States have indeed been practicing the acute care surgery paradigm for decades, dating back to the pioneering work by John Border in the 1970s. Similarly, European countries have historically endorsed the analogy of the "combat surgeon" model which evolved in the aftermath of the Franco-Prussian War in 1870. In the twentieth century, Germany took a leadership position as a driver of integrated trauma care. This "European model" is reflective of the notion that trauma represents a disease of its own, rather than just the sum of specific injuries, and should therefore be managed by one single specialist—the trauma surgeon. The "Hannover school" founded by Harald Tscherne in the 1970s was further refined under Otmar Trentz in the 1990s who established trauma as a true scientific research-based discipline with an impressive measurable impact on the quality of trauma care and on patient outcomes. Academic institutions in Italy have recently taken a leading position in Europe by driving best practice guidelines in trauma and acute care surgery. In support of this statement, this first-edition textbook is preeminently written by Italian authors and edited by four distinguished experts from renowned institutions in Italy. The groundbreaking work provides a compelling testimonial on the current state of research and innovation in the field. This essential textbook will hopefully contribute to the prioritization and optimization of multi-disciplinary protocols and standardized processes for managing the vulnerable population of critically ill and severely injured patients. The editors have to be commended for mastering the gargantuan task of providing a compelling overview on all pertinent disciplines in trauma, acute care surgery, and emergency general surgery, by integrating these distinct entities in an elegant fashion into a new and invaluable "bible" for clinicians.

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Part I

General Principles

1

Surgical Education and Training for Emergency Surgery and Surgical Specialties

Antonello Forgione and Salman Y. Guraya

Key Points

- The aim of a standard surgical training program is to provide a competent surgeon, trained and assessed by an effective curriculum, who is ready for unsupervised practice.
- Several assessment tools are available in the workplace-based assessment strategy such as direct observation of procedural skills, mini-CEX, case-based discussions, and objective structured clinical examination (OSCE).
- A myriad of state-of-the-art surgical training tools is available for the trainees and senior surgeons that can serve the purpose of complementing the accredited surgical residency programs outside the OR.
- Simulation carries the promise to promote experiential learning, to secure patient safety, and to recreate scenarios that are rarely encountered and can assess the trainees' skills and competence in diverse situations.
- The mechanical box simulators are designed as boxes with objects or organs that are accessed using surgical instruments. The quality of the tactile feedback is perceived to be the same as in the OR, and the surgical performance can be monitored by trained surgeons.
- Telemedicine sweeps away distance barriers and can provide sufficient expertise to novices in remote rural areas. This innovative technology provides a high-definition profile of operative field, allows verbal communication between the mentor and mentee, and allows the trainer to point on the screen for further operative steps.

1.1 Introduction

Training and education of the surgical trainees is a dedicated, expensive, and demanding exercise that needs continuous supervision and transfer of surgical expertise in a structured fashion. This phenomenon envisages a myriad of learning tools, technologies, opportunities, and stakeholders [1]. The aim of a standard surgical training program is to provide a competent surgeon, trained and assessed by an effective curriculum, who is ready for unsupervised practice. This produce of an accredited surgical training program shall be able to function independently through an effective collaborative interprofessional practice that is known to have a positive impact on the delivery of health-care system, enhances patient satisfaction, reduces medical errors, and promotes efficiency and appropriate use of health services [2]. Such training programs must also ensure that the trainee surgeons develop the right personality, attitudes, and skills who can deliver with exceptional leadership capabilities in the high-tech operating rooms equipped with cutting-edge technologies [3, 4].

The orthodox apprenticeship approach of surgical training, where trainees would learn incidentally from their supervisors while essentially delivering service, is no longer sustainable due to major flaws such as unstructured training in a noneducational environment. Furthermore, the absence of a robust workplace-based assessment model leads to inadequate supervision of the trainees with insufficient feedback and ineffec-

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tive assessment [5, 6]. Several assessment tools are available in the workplace-based assessment strategy such as direct observation of procedural skills [7], mini-CEX [8], case-based discussions [9], and objective structured clinical examination (OSCE) [10]. Of these, DOPS and OSCE carry a great potential for assessing the surgical competencies in a supervised learning environment with the possibility of immediate feedback. Traditionally, operating room has been the center-point of surgical training and has been considered as a stand-alone trusted platform for surgical education. However, in the recent past, the landscape of surgical training environment within which surgical education takes place has significantly changed due to the incorporation of ambulatory care, day-care surgery, computer-integrated surgery, concerns about patient safety, operating time, quality control, and ethical issues [11, 12].

The surgical rotations in accredited residency programs do not essentially articulate well with the career goals of the learners, ending up with less satisfied learners and suboptimal placements. In view of these shortcomings, parallel surgical training programs and modalities are needed that can bridge educational gaps within the context of skills [13]. In addition to the overarching need for adjuvant training conventions for the surgical trainees, there is also pressing need to provide surgical training opportunities to the trained and established surgeons. This urge to update the skills of surgical trainees will allow them to synchronize and modernize their skills with the evolving surgical technologies and emerging protocols. Unfortunately, there is dearth of evidence that can shed light on such surgical educational programs. In addition, the literature fails to provide a stand-alone comprehensive platform that can help the surgical trainers and trainees to fulfill their professional desire to accomplish surgical competence and to update their surgical skills. This book chapter explicitly sheds light on the current state-of-the-art modern surgical educational tools and programs with the aim to provide a precise note on merits and demerits of each modality.

1.2 Surgical Education and Training for Emergency Surgery

The sensitivity and presentation of patients in emergency room [14] necessitate instant lifesaving action plans by physicians that not only require clinical competence but also depend upon the physician's personality and character [15]. Periodic and systematic examinations have the potential to enhance the quality of patients' care and satisfaction and tend to reduce patients' stress in the ER [16]. Such unique approaches demand a multidimensional set of competencies that should be inculcated in ER physicians for developing their core skills in professional domains. These opportunities should be provided to them during the preclinical and clinical years.

The International Federation for Emergency Medicine (IFEM) has developed a 4-year structured universal standard curriculum for emergency medicine that can be conveniently embedded in the medical curricula [17]. This curriculum has been designed by an international consortium of specialists, health-care experts, and physicians and includes core domains of teaching emergency medicine to medical students. The key focus remains on improving the fundamental knowledge of clinical sciences employed in emergency medicine such as acquiring basic life-support cardiopulmonary resuscitation skills, to institute therapy of first aid for airway obstruction, to manage all types of shocks in all age groups, to administer cerebral resuscitation in brain illness and injury, to initiate basic principles of stabilization in life-threatening illness or injury, and to help the students to develop professional behavior, probity, and communication skills. The surgical components of IFEM curriculum emphasize on emergency management of trauma to all regions of the body including head and neck, chest, abdomen, musculoskeletal, vascular, urological, and dental trauma. Another body with a more precise focus on surgery, recognized as the European Society for Trauma and Emergency Surgery (ESTES), aims to advance the professional practice of emergency and trauma surgery right from the prehospital care through diagnosis, intervention, and intensive care to rehabilitation [18]. The core contents of the ESTES teaching model envisages to enable students to be competent in disaster and military surgery, emergency surgery, polytrauma and visceral surgery, and sports and skeletal trauma. In partnership with the German Society for Orthopedics and Trauma Surgery, ESTES offers a DGOU fellowship program that endeavors to provide the clinical and scientific training, medical education, and clinical exchange among the European nations.

The American College of Surgeons (ACS) offers an accredited certification as the Fellow of the American College of Surgeons (FACS) to all surgical specialties including emergency and trauma surgery [19]. The fellowship program entails submission of application and evaluation of the applicant's professional career. The grant of fellowship is based on the evaluation reports about the candidate's professional competence, ethical conduct, and surgical judgment. Since the eligibility to apply demands that the applicant should have a postgraduate certificate and should be a practicing surgeon, the FACS per se does not directly evaluate the surgical competence of the candidate; rather it relies on the feedback from supervisors and licensing bodies. It is commonly perceived that the working climate between the surgeon and his technical staff in the operating room performs optimally when this hierarchy is diligently followed by all stakeholders [20]. The Advanced Trauma Operative Management (ATOM) by ACS is an effective educational tool for enhancing surgical competence of trainees in the operative management of penetrating injuries to the abdomen and chest [21]. The ATOM course consists of six 30-min lectures followed by a 3-h lab session. The lectures entail penetrating trauma management by trauma laparotomy for injuries of the spleen and diaphragm;

liver, pancreas, and duodenum; and genitourinary and cardiovascular systems. The lab sessions consolidate the knowledge gained by theoretical sessions in the form of hands-on surgical management of the aforementioned injuries.

1.2.1 The Pitfalls and Challenges in Harmonizing a Universally Accredited Curriculum for Emergency Surgery

In the wake of scattered and non-integrated curricula and programs for emergency surgical training, there is pressing need to understand the value and place of such courses that can be embedded into MBBS curricula. On the basis of the community needs, resources, and faculty expertise, the medical educators would be able to incorporate a horizontal or, preferably, a vertical integration. For the postgraduate accredited residency programs, there is a dearth of a standard emergency surgery curriculum. The absence of an internationally acceptable program eventually deters the migration of international graduates across regions and countries due to varying contents, credit hours, and the level and depth of training they attain. A universally acknowledged curriculum for emergency surgery can be produced by an int'l consortium of field experts that can address the core contents and learning objectives across the globe.

1.3 Surgical Education and Training Tools

A myriad of state-of-the-art surgical training tools is available for the trainees and senior surgeons that can serve the purpose of complementing the accredited surgical residency programs outside the OR. The following section elaborates some of the surgical education tools and models using modern, cutting-edge technologies being used across the world.

1.3.1 Simulation-Based Surgical Tools

Literature has shown that as much as 10% of the admitted patients encounter various forms of unwanted surgical complications due to human error [22]. Unfortunately, the orthodox surgical practice of "see one, do one, teach one" approach exposes patients to inexperienced trainees that endanger patients' health and safety [23]. Henceforth, the surgical trainees can no longer rely only on human beings to attain their skills with the potential of trial and error. This necessitates the urge to explore, define, and implement versatile surgical educational models that do not jeopardize patient safety [14]. One such model implies simulation that refers to "a technique to replace or amplify real patient experiences with guided experiences, artificially contrived, that evokes or replicates substantial aspects of the real world in a fully interactive manner" [24]. Simulation carries the promise to promote experiential learning, to secure patient safety, and to recreate scenarios that are rarely encountered [25] and can assess the trainees' skills and competence in diverse situations [26].

The two most commonly used simulation-based surgical training models are described hereunder in detail.

1.3.1.1 Mechanical Simulators

The mechanical box simulators are designed as boxes with objects or organs that are accessed using surgical instruments [27]. The novice surgeons, starting to learn laparoscopic skills, can practice on synthetic materials as well as animal organs or tissues [28]. The quality of the tactile feedback is perceived to be the same as in the OR, and the surgical performance can be monitored by trained surgeons. A more refined version of commercially available mechanical box simulators is LapSim virtual reality simulator that is perceived to carry high fidelity with more precision [29].

1.3.1.2 Virtual Reality Simulators (VRS)

The VRSs facilitate the surgical trainees in developing their psychomotor skills and manual dexterity and in recreating the OR environment without supervision or time constraints. These modern surgical tools permit the learners to acquire the required skills with confidence at their own learning pace [30]. Modern VRSs such as the well-recognized MIST-VR and the newer LapSim (Surgical Science, Gothenburg Sweden) have built-in abstract graphics than can provide a high-fidelity simulation for trainees and assessors [31]. The commercially available laparoscopic VRS software replicate tasks such as grasping, cutting, and suturing, which help the trainees to acquire psychomotor skills essential to perform real-time procedures [32].

1.3.2 Video Games

There is growing evidence that video games have a positive effect on sharpening the basic laparoscopic surgical skills [33]. Apart from the numerous negative impacts of excessive game playing [34], several studies have argued that video gaming promotes spatial attention and hand-to-eye coordination [35]. The trainees invariably encounter technical challenges during laparoscopic surgery such as loss of depth perception, haptic feedback, and fulcrum effect [36]. Video games have the potential to overcome these barriers by providing a cost-effective and widely available surgical training tool for developing cognitive skills [37]. Despite these promising signals, there is currently, however, no standardized method to assess that video games are effective in transferring the desired surgical skills that are comparable to the OR experience.

1.3.3 Animal Lab Simulation

Labs using animal models provide substantial support in surgical training, education, and research. At the same time, animal labs offer a useful platform for the initial applications of innovative technique [38]. Live animal surgery remains the best training model, offering high fidelity that is unmatched by other kinds of simulation models [39]. From the medicolegal perspective, the use of animal labs is considered where no reliable alternative for surgical training and education is available. Nevertheless, in such situations, implementation of the legislative framework about 3 Rs, "Refine the procedure to limit suffering, Reduce the number of animals to a minimum, Replace the use of animals with non-animal alternatives when appropriate," should be closely adhered to [40].

1.3.4 Cadaveric Lab Simulation

Training of surgical skills on cadavers offers the best anatomy realism that can effectively prepare the trainee before working on living human beings [41]. Research has shown that surgical training on human cadaver model significantly augments reality simulation for the acquisition of laparoscopic colorectal skills. Thus, although difficult, the human cadaver model is perceived to be better acknowledged than simulators for laparoscopic sigmoid colectomy [42]. There is abundance of evidence that the simulator-based training followed by cadaver training can be conveniently integrated into surgical learning curve [43].

1.4 Mini-fellowship Surgical Training Programs

Well-crafted structured mini-fellowship surgical training programs, tailored to the needs of practicing surgeons, containing hands-on operative and clinical sessions have shown strong potential in transferring the desired laparoscopic surgical competence [44, 45]. A mini-fellowship surgical training program was successfully employed at the AIMS Academy that included telementoring sessions in the remote area of Russia [46]. The key highlights of this program reflect that, for being a competent surgeon, the acquisition of technical competence is as important as the attainment of clinical knowledge. Exploring the effectiveness of another surgical training program, Jenkins et al. studied a proficiency-based structured task-specific training model for laparoscopic colorectal surgery, and the authors have proposed that multimodality training with a modular operative approach substantially shortened the time to gain proficiency with low morbidity with an error rate of 25% [47]. Nevertheless, Simpson and Scheer have argued that all such mini-fellowship programs should have a standard set of program evaluation that can constantly evaluate its impact on trainers and trainees [48].

1.5 Preceptoring and Proctoring for Surgical Training

Preceptoring refers to the situation when an experienced surgeon scrubs with the learner to supervise the surgical procedure or is ready to intervene. In contrast, a proctor is a supervisor who monitors surgery, shares advice, and intervenes when necessary. Preceptoring is often employed before the trainee has attained the intended surgical skills for a given surgical procedure. Because of the growing concerns about the ethical and medicolegal issues, preceptoring permits training on patients while adhering to the standards set forth for patient safety [49].

1.6 Telementoring for Surgical Training

Telementoring refers to "the process of remote guidance and technical assistance to surgical procedures, utilizing telecommunication techniques" [50]. Telemedicine sweeps away distance barriers and can provide sufficient expertise to novices in remote rural areas. This innovative technology provides a high-definition profile of operative field, allows verbal communication between the mentor and mentee, and allows the trainer to point on the screen for further operative steps [51]. Since the mentoring process is not restricted by distance, the costs of formal mentoring programs may be reduced, and remote assistance can be incorporated into formal training schedule [52]. Forgione et al. developed a comprehensive theoretical and practical min-fellowship program that incorporated telementoring mode of training at the Advanced International Mini-invasive Surgery Academy at Milan, Italy [46]. A Russian surgeon, after successfully passing the required theoretical and practical sessions at AIMS, was telementored at the Northern Medical Clinical Centre Arkhangelsk Russia, about 2868 km from Milan, by experts from AIMS Academy Milan. Several other successful telementoring training events have been reported from across the world [53–55].

1.7 Telerobotic Manipulation and Assistance

By using Zeus TS micro joint system (Computer Motion Inc., Santa Barbara, CA), an expert robotic surgeon can provide telepresence for trainee surgeons in rural and

Table 1.1 Advantages and disadvantages of the commercially available surgical training models

No.	Surgical training model	Advantages	Disadvantages
1	Mechanical simulator	• Reproducible • Standardized • Training of isolated skills • Cheap	• No high fidelity • No tissue rendering
2	Virtual reality simulator	• Performance of real operations • Evaluation of isolated skills • Instant objective feedback	• Expensive • Questionable software and interface reliability
3	Animal lab	• Easy availability • Good tissue handling	• Ethical issues • Expensive
4	Cadaver lab	• High fidelity • Same anatomy (included individual variation) • No time pressure	• Ethical issues • Limited availability • Non-compliant bloodless tissues
5	Telementoring	• Exact anatomy • Realistic bleeding • Real OR setting • Independence of first operator	• Requires another surgeon throughout surgery • Expert surgeon cannot operate directly
6	Telerobotic assistance	• Exact anatomy • Realistic bleeding • Real OR setting	• Expensive • Requires another surgeon throughout surgery • Pressure of training

remote areas across the world. The telerobotic expert can guide intraoperatively at a remote site, looking at the same images as the primary surgeons, as both are located outside the surgical field [56]. Following the principles of telerobotic assistance for surgical training, Anvari et al. established the world's first remote telerobotic surgical service by connecting St Joseph's Hospital in Hamilton and North Bay General Hospital, situated about 400 km north of Hamilton. Twenty-one telerobotic laparoscopic operations were performed without any intraoperative complication. The investigators have argued that refinements in the robotic and telecommunication technology can offer a platform for routine use of the state-of-the-art laparoscopic surgical practice in rural communities that can be run by a close collaboration between surgeons in high-volume tertiary and rural hospitals.

The key features of all described surgical educational modalities along with the advantages and disadvantages are elaborated in Table 1.1.

1.8 Objective Assessment of Technical and Nontechnical Surgical Skills

1.8.1 Objective Structured Assessment of Technical Skills (OSATS)

A fundamental element of the accredited surgical training is an objective and meticulous assessment of the surgical trainee. Unfortunately, owing to variations in understanding and diverging parameters used by assessors, there has always been low validity and reliability by subjective assessment of any skill or competence. On the contrary, objective assessment follows a precise and explicit track with no room for personal judgment by the assessors. OSATS is a valuable objective assessment tool that can provide both a holistic and in-depth evaluation of open surgical skills [57]. This modality contains standard assessment forms with pre-defined criteria indicating how to score performance in the technical domain.

1.8.2 Fundamentals of Laparoscopic Surgery [58]

FLS, a joint consortium developed by SAGES and the American College of Surgeons, aims to teach and assess the knowledge, judgment, and skills inherently required for laparoscopic surgery, independent of the surgical specialty [58]. During the assessment, a physical endotrainer box simulator is used. "The optical system shows a monocular view of a series of objects that must be manipulated to perform five tasks of increasing complexity; peg transfer, cutting/dissecting, placement of a ligating loop to secure a tubular structure, and intra-corporeal or extra-corporeal knot tying" [59]. A trained proctor supervises this process and awards marks to each task. FLS offers a convenient and feasible tool for teaching laparoscopic surgery with an added advantage of being a validated assessment modality [60].

1.8.3 Fundamentals of Endoscopic Surgery [2]

Flexible endoscopy is a key component of surgical practice as surgeons perform upper and lower GI endoscopy during the preoperative work-up, intraoperative evaluation, and postoperative to identify the anatomic changes induced by surgical intervention [61]. The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) and the American Board of Surgery have jointly developed FES curriculum, a comprehensive educational tool very similar to FLS that includes Web-based didactic component of flexible endoscopy containing 12 units of teaching domains, written multiple choice exam (cognitive component), and a 5-module virtual reality skills exam (hands-on component).

1.8.4 Fundamental Skills for Robotic Surgery (FSRS)

FSRS has been validated as an effective, feasible, and structured curriculum that verifies its effectiveness by remarkable advancements in basic robotic surgery skills [62]. The system involves a simulation-based robotic curriculum that can be conveniently embedded in surgical training and educational programs.

1.8.5 Measuring Nonsurgical Skills: The Nontechnical Skills for Surgeons

Surgical educators have agreed that critical, cognitive, and interpersonal skills of surgeons significantly complement surgeons' technical abilities [63]. The Surgical Team Assessment Record (STAR) is one of the instruments that is designed to evaluate the human behaviors in the OR [64]. This scale attempts to determine the organizational, situational, team, and personal factors that might influence the surgical performance in the OR. A surgeon's intraoperative nontechnical skills are strongly correlated with the surgical outcomes, and breakdowns in surgeon's behavior in the OR negatively affect nontechnical characteristics such as teamwork, leadership, communication, confidence, and decision [65]. This emphasizes the need to embed fundamental domains of NOTSS such as communication, decision-making, situation awareness, leadership, teamwork, professionalism, and task management into the existing surgical training curricula [3, 66, 67]. Education and assessment of nontechnical skills in surgery lead to enhanced surgeons' performance in the OR that will improve quality as well as patient safety [4, 68].

Policymakers and surgical educators are increasingly incorporating virtual and e-Learning tools into the surgical training, and the distance learning arm of these modalities makes e-Learning more attractive and feasible. However, the fidelity and effectiveness of surgical educational platforms and training centers in delivering the desired skills by online video libraries and e-Learning platforms needs to be tested and validated by accrediting bodies.

1.9 Trainees' Perceptions of Surgical Education Tools and Strategies

While training the surgical residents and practicing surgeons, its customary to deeply understand the preferred resources of surgical education as desired by the learners. This understanding is driven by the fact that each learner has a distinct learning style and identification of these unique learning preferences can help trainers in improving the delivery of surgical education [69]. Guraya et al. explored the preferred learning resources of the participants attending surgical courses at the AIMS Academy during 2010 to 2013 and noted that the majority of participants (467/636; 73%) preferred "direct experience in the OR" as their favorite learning strategy, followed by "tutoring by skilled trainer" proposed by 426/636 respondents [13]. The study had concluded that surgical trainees preferred hands-on training and mini-fellowship courses for enhancement of their surgical skills.

In the later section of this article, we have described few popular surgical training centers.

1.10 State-of-the-Art Surgical Training and Education Centers

Some of the most popular surgical education and training centers, worldwide, that offer training services both in "dry and wet labs" using world-class laparoscopic instruments using theoretical as well as practical learning sessions are shown in Table 1.2. The l'Institut de Recherche contre les Cancers de l'Appareil Digestif (IRCAD) offers the opportunity to train with animals, while the UK centers use cadavers, as animal surgical training is forbidden. The AIMS Academy is a state-of-the-art training venue for hands-on surgical training along with the opportunity for in-campus and telementoring laparoscopic surgery courses and fellowship programs.

The commonly accessed online resources for surgical education and training are provided by WebSurg, SAGES Online, European Association for Endoscopic Surgery (EAES), and American Society for Gastrointestinal Endoscopy (ASGE). A host of recorded videos by field

Table 1.2 World's most popular surgical training and education centers

No.	Training center	Country
1	IRCAD[a]	Strasbourg, France Taichung, Taiwan Barretos, Brasil
2	AIMS[b]	Milan, Italy
3	Minimal Access Therapy Training Unit (MATTU) Centre	Guilford, UK
4	Cuschieri Skills Centre	Dundee, UK
5	Methodist Institute for Technology, Innovation and Education (MITIE)	Houston, USA
6	Center for the Future of Surgery	San Diego, USA
7	European Surgical Institute	Norderstedt, Germany

[a]l'Institut de Recherche contre les Cancers de l'Appareil Digestif
[b]Academy for International Minimally Invasive Surgery

experts with insightful remarks at key surgical steps along with a range of theoretical knowledge-based material make these portals extremely useful for the surgical trainees and practicing surgeons.

Conclusion

Financial constraints, quality control, and patient safety have urged the surgical educators to explore and develop more cost-effective, state-of-the-art surgical educational platforms that can be employed outside the OR. Simultaneously, the practicing senior surgeons are desired to periodically refresh and update their surgical skills that will allow them to get acquaintance with the modern surgical technologies. A myriad of cutting-edge technical innovations are now commercially available such as the simulation-based mechanical and virtual reality simulators, animal and cadaveric labs, telementoring, telerobotic-assisted surgery, and video games. The existing world-renowned surgical training centers employ various clusters of training tools that aim to embed the acquisition of surgical knowledge and technical skills. This research demands the initiation of concerted efforts in developing a blended and unified structured surgical training program that can be employed across the world.

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Pathophysiology of Acute Illness and Injury

2

Sergio Arlati

Key Points

- The inflammatory reaction is a highly adaptive, integrated response with a global protective effect against microbial pathogens or tissue damage. It provides for the elimination of pathogens, removal of cellular debris, and promotes tissue repair and healing.
- Multiple trauma or severe infection causes a widespread inflammatory reaction that causes diffuse endothelial activation (chemotaxis), damage (permeability edema), and vasodilation (hypotension-shock).
- Inflammation and coagulation are strictly coupled. As a general rule hyperinflammation means hypercoagulability. Coagulation has beneficial effects when inflammation is localized, but it becomes catastrophic when disseminated intravascular coagulation ensues.
- Humoral inflammatory mediators include cytokines, complement, thrombin, acute phase proteins, kinins, and PAF. Endothelial cells, monocytes, antigen-presenting cells (macrophages and dendritic cells), and neutrophils are the main effector cells.
- Neutrophils are responsible for tissue damage. Their widespread activation accounts for the noxious effects to innocent tissues with multiple organ damage.
- A counter-inflammatory response mounts immediately after the hyperinflammatory reaction. Such response is proportionate to inflammation along the whole course of disease.
- An immediate decrease of the acquired (lymphocytic) immune response occurs in parallel with inflammation leading to dysfunction and progressive immunoparalysis.
- Apoptosis of the cells of the immune system is the main responsible of immunoparalysis. This exposes to increased risks for opportunistic infections and sepsis/septic shock.

2.1 Basic Concepts

The pathophysiology of acute care illnesses is a generalized, multi-systemic process that invariably activates the immune-inflammatory and coagulation systems with production of diffuse tissue and organ damage. The temporal development of acute care illnesses is quite variable although it usually evolves as a multiphasic process or more rarely as a single acute event that the body can't cope with. For example, multiple trauma causes the activation of the immune-inflammatory, coagulation, and neuroendocrine systems. Thus ischemia-reperfusion that follows severe post-traumatic hemorrhage with hypotension and tissue hypoperfusion activates the immune-inflammatory system with adhesion of polymorphonuclear leukocytes (PMNs) to the endothelium and increased capillary permeability, plasma fluid leakage, and tissue edema. The widespread activation of the coagulation creates a prothrombotic milieu with deposition of microthrombi, diffuse capillary obstruction, and further ischemic damage. Similarly, severe pneumonia challenges the circulating monocytes and resident tissue macrophages with a broad spectrum of microbial molecules. The subsequent activation of the inflammatory and coagulation systems causes the widespread activation of the endothelium with production of either local (e.g., ARDS) or distant organ damage (multiple organ dysfunction syndrome, MODS). However, the immune system provides a counter-regulatory response that limits the deleterious effects of the generalized inflammatory activation

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(compensatory anti-inflammatory response syndrome, CARS) [1]. Although CARS opposes to the systemic inflammatory response syndrome (SIRS) [2], this is a double-edged sword because the risk of septic complications is increased. If unresolved, SIRS and CARS become the underlying players of a catabolic syndrome that leads to MODS and ultimately death [3]. In the past SIRS was viewed as an exaggerated response to inflammatory stimuli, but the latest experimental and observational data indicate that it is a rather predictable side effect of especially severe morbid events. In practice, SIRS and CARS result from the growing sophistication of ICU care that keeps patients alive during the early (acute) phase of traumatic and septic diseases. The protracted survival of formerly rapid lethal conditions makes now appreciable their natural evolution. Recent acquisitions also suggest that SIRS and CARS develop simultaneously rather than in sequence as previously believed. As a result a mixed antagonist response syndrome (MARS) was coined to reflect the balance between SIRS and CARS [4] (Fig. 2.1).

However, the phenotypic predominance of the hyperinflammatory state is the rule in early sepsis, hypoxia, or trauma as influenced by antigenic load, microbial virulence, host genetic factors, age, nutritional status, and comorbidities [5]. In the past CARS was believed to develop after SIRS exhaustion by repeated noxious stimuli (second hit theory) [5, 6]. According to this theory, recurrent morbid insults augment the inflammatory response by repeated stimulation of the inflammatory cascade. In this sense, SIRS would no longer depend by the initial insult but rather by the intensity and frequency of subsequent hits. However, the continuous challenge of the inflammatory system mounts an anti-inflammatory response that ultimately becomes predominant. So CARS does not develop simultaneously with SIRS, but only a minimal overlap would exist between the two phenomena. This pathophysiological view is derived from the observation that CARS prevails in the later stages of disease when the increased susceptibility to infections is associated with a weakened pro-inflammatory response (SIRS exhaustion). This concept translated into the linear transition from acute (early) SIRS to chronic (late) CARS with possible alternating recurrence of the two phases (MARS), (Fig. 2.2).

However, this view is no longer accepted as the historical belief of the “cytokine storm” after a catastrophic acute illness (e.g., meningococcal sepsis) giving the spectacular inflammatory reaction is not the rule [7]. Instead, the most common picture is by far a patient over 65 years of age with sepsis or recovering from multiple trauma/surgery and evidence of immunosuppression without the typical exaggerated acute phase inflammatory response [7]. In the past “cytokine storm” was synonymous of SIRS that is hyperinflammation defined by excessive release of classical pro-inflammatory cytokines including IL1, IL6, IL8, and TNFα. However, this concept is too narrow as it was quickly noted that “cytokine storm” is not the typical occurrence in late (chronic) sepsis or even in acutely septic patients with a weakened immune system [8, 9]. Similarly, it seems incorrect to define CARS on the basis of elevated release of anti-inflammatory cytokines in the blood. The current concept is rather that the magnitude of cytokine release depends on the premorbid immune-inflammatory status of the patient [10]. Otherwise stated the healthier the patient, the stronger will be the release of cytokines after stimulus. As a corollary, the more protracted is the disease, the more faded will be the inflammatory response over time (e.g., recurrent sepsis in postsurgical or trauma patient). However, an acute inflammatory response although typical of the acute phase may occur at any time of the disease profile if the host is sufficiently immunologically responsive. This view holds for

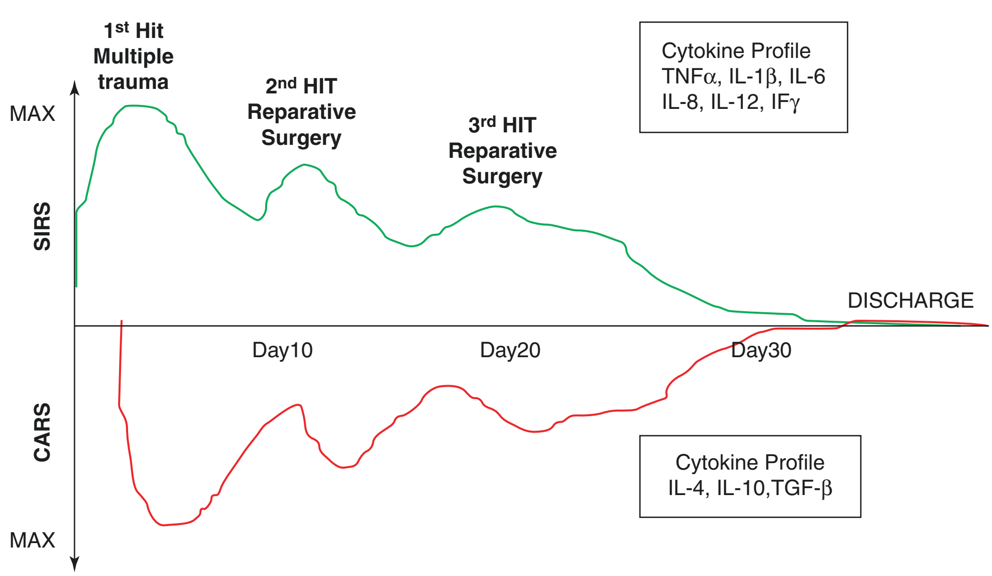

Fig. 2.1 Temporal profile of pro-inflammatory and anti-inflammatory cytokines according to the most recent hypothesis of simultaneous development of SIRS and CARS. So MARS is always ongoing

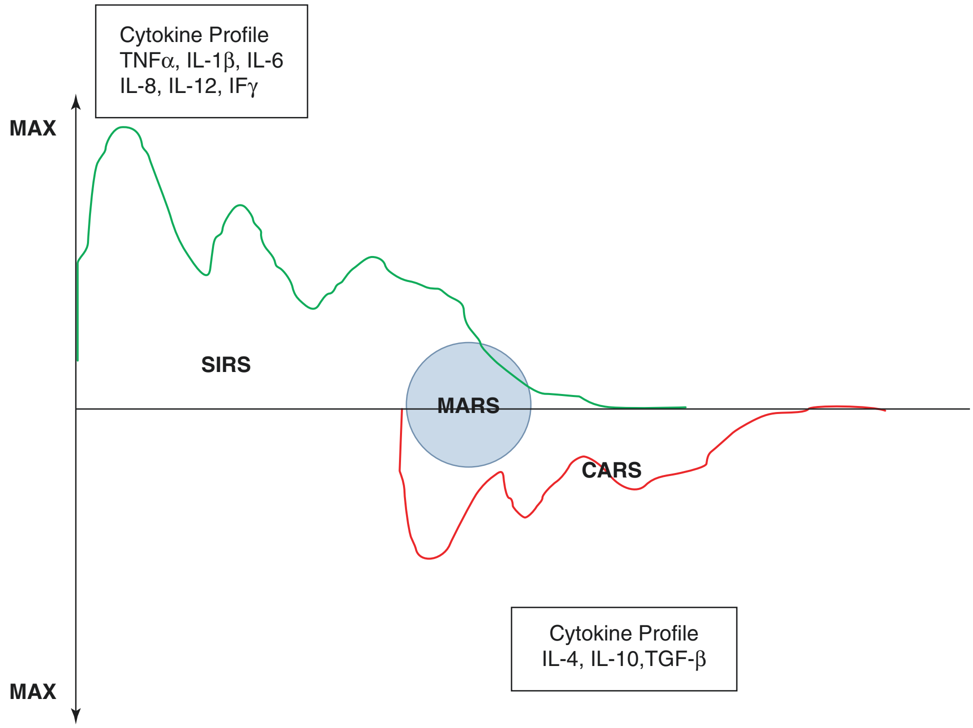

Fig. 2.2 Temporal profile of pro-inflammatory and anti-inflammatory cytokines according to the hypothesis of sequential development of SIRS and CARS. MARS is a transitional state in-between them

both the pro-inflammatory and anti-inflammatory cytokines, so it is incorrect to define the patient's inflammatory status on the basis of his/her cytokine profile [10]. Therefore, the mixed cytokine response pattern better represents the patient's inflammatory status leading to the paradigm "Sepsis: Always in MARS" [11]. Thus a hyperinflammatory status at the onset of sepsis or multiple trauma reflects the ability of the host to release a great amount of pro-inflammatory and anti-inflammatory mediators. Such ability is destined to fade over time with progression to a late (chronic) inflammatory status. In recent years, the immuno-competent cells have emerged as a new relevant player for the appearance of immunosuppression or immunoparalysis that often characterizes the host's response during the more chronic disease stages. At present, the process of immuno-suppression (decreased T-cell proliferation and production of IL2, decreased monocyte and macrophage function) is believed to occur in parallel with the hyperinflammatory status of early sepsis of traumatic or surgical origin [12, 13]. Animal studies indicate that in non-survivors, the immune cell suppression progresses indefinitely up to anergy from the very beginning to the more chronic stages in a time-independent manner [10]. As a result, the phenotype of immunosuppression does not often correspond to the cytokine pattern of peripheral blood.

Prior to early deaths, cellular immunosuppression develops rapidly together with high pro-inflammatory and anti-inflammatory cytokine release (MARS-like) [14]. Conversely, the chronic state is preceded by a progressive (subacute or chronic) impairment of immune cells function with robust pre-lethal signs of anergy and a deteriorating but MARS-like cytokine profile (simultaneous presence of both pro-inflammatory and anti-inflammatory mediators in the blood) [10]. The spread of the inflammatory process starting from a single organ or tissue is by far the most frequent event in the pathophysiology of acute diseases. The inflammatory response is a highly coordinated process, which has evolved to limit the spread of noxious stimuli, eliminates pathogens and necrotic cellular debris, and promotes the healing of damaged tissues. It is subjected to multiple activations and control mechanisms and whose efficiency is largely dependent on genetic predisposition, age, and neurovegetative and hormonal milieu derived from the stress response. Finally, inflammation and immunity are tightly related in a complex network of multiple interconnections and reverberating loops. However, extremely intense or repeated stimulations may disturb their tuned response so that the inflammatory mediators spill over the anatomical barriers and multiple organs dysfunction syndrome ensues. Cardinal inflammation phenomena are local vasodilation, increased endothelial permeability, and chemotactic cells activation from the natural (granulocytes and monocytes) and acquired immune system (lymphocytes). The vascular mechanisms that lead to the four cardinal signs of inflammation are resumed in Fig. 2.3.

Neutrophils and monocytes are activated to infiltrate the site of infection with subsequent phagocytosis and lysis of bacterial products or cellular debris. In the meanwhile, the activated coagulation system seals the site of inflammation and provides a meshwork of fibrin that helps in the reparation process. Therefore, increased membrane permeability,

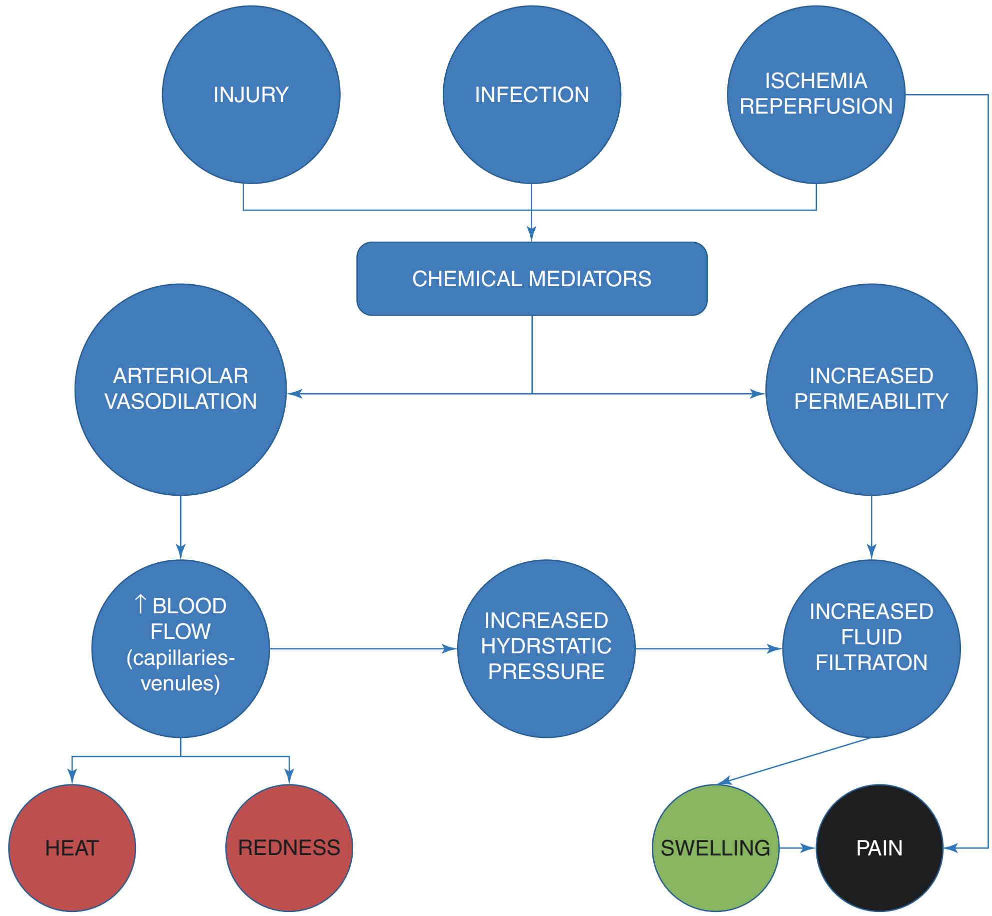

Fig. 2.3 Vascular mechanisms at the origin of the cardinal signs of inflammation. Arteriolar vasodilation and increased permeability are responsible for augmentation of blood flow (redness and heat) and fluids accumulation in tissue (swelling and pain)

capillary vasodilation, chemotaxis, and phagocytosis are defensive mechanisms that act in concert to ensure the maximum of protection against any threat or danger. A multiplicity of cell types (e.g., endothelium, monocytes, platelets) as well as humoral factors (complement, leukotrienes, kinins) acts following a synergistic and often redundant logic to activate, propagate, and maintain the inflammation so that the host defense is guaranteed. Nevertheless, the uncontrolled diffusion of inflammatory mediators causes hypotension and tissue edema by generalized vasodilation and increased endothelial permeability. Furthermore, the diffuse deposition of microthrombi by disseminated intravascular coagulation worsens the oxygen supply to tissues this, in turn, contributing to ischemic cells damage, further inflammation (ischemia/reperfusion injury), and MODS. The local action of the inflammatory system is similar to a well-refined military strategy. After an enemy attack (e.g., trauma) that engages the local garrison (resident macrophages and glial cells), the combat zone is rapidly enclosed and sealed by reinforcement troops (chemotactic activation of PMNs and intravascular coagulation). Thereafter, the soldiers get into the battlefield (increased membrane permeability and leukocytes migration) and shoot at the enemy destroying him (phagocytosis, proteases, and toxic oxygen products). However, after a massive attack, the hurried and often disorganized mobilization of the reserve troops makes difficult or even impossible to implement an effective defense. The recruitment of soldiers is often chaotic and uncoordinated (widespread chemotactic activation), the effective concentration of troops is impossible (generalized increase of endothelial permeability), and military patrols often shoot at innocent people (organ damage). Thus, pneumococcal pneumonia can transform into severe sepsis or septic shock if a generalized inflammatory reaction develops by either cellular (neutrophils, monocytes, macrophages, endothelium) or humoral effectors (complement, contact phase proteins, leukotrienes, cytokines, chemokines) resulting into increased capillary permeability (tissue edema), vasodilation (hypotension), and coagulation activation (ischemic organ damage). Generally, the pathophysiological mechanisms that lead to a systemic inflammatory reaction are infections, trauma, and ischemia-reperfusion damage. Each of them can act by itself or in combination with the other two. For example, multiple trauma causes the activation of immune-inflammatory mechanisms by itself (tissue necrosis), or as a consequence of ischemia-reperfusion damage (e.g., gut ischemia by post-traumatic mesenteric hematoma or post-ischemic muscular tissue reperfusion after hemorrhagic shock). Apart from the abovementioned mechanisms, the uncontrolled activation of the immune system (autoimmune diseases), massive cytokines production (metastatic cancer, leukemia, or lymphoma), and the unrestrained activation of serum proteases (acute pancreatitis) are less frequent causes of generalized inflammatory activation.

2.2 How the Systemic Inflammatory Reaction Develops

The widespread activation of the inflammatory system (systemic inflammatory reaction syndrome, SIRS) originates from the site of trauma, infection, or hypoxic cell damage (ischemia/reperfusion). Infection, traumatic or hypoxic injury, causes the release of a heterogeneous pattern of endogenous and exogenous molecules that trigger the innate immune system as chemoattractants and activators of antigen-presenting cells.

2.2.1 Alarmins

Infection from bacterial, viral, and fungal agents releases signaling substances that are recognized by the innate immune system due to their characteristic molecular pattern (pathogen-associated molecular patterns, PAMPs) [15]. Conversely, traumatic or hypoxic cell injury releases the so-called damage-associated molecular patterns (DAMPs) [16, 17] which represent the correlate of PAMP for danger signals of endogenous origin. PAMPs and DAMPs are grouped into the larger family of "alarmins" in assignment to the term danger signals [15]. Otherwise stated PAMPs and DAMPs constitute a physiologic signaling system that alerts the body to the presence of foreign invaders or noxious stimuli. "Alarmins" activate specific receptors of the superfamily of the Toll-like receptors (TLRs) [18, 19], expressed on endothelial and innate immune cells like macrophages, dendritic cells (antigen-presenting cells, APCs), monocytes, and PMNs [20]. APCs act as an intermediate between innate and acquired immune system. Their main function is to process antigen material and to present it to effector T cells of the immune system. TLR receptors recognize a variety of peptides that are important signaling molecules for activation and production of a multiplicity of inflammatory mediators. In addition, DAMPs are potent activators of the complement system [21–23] whose anaphylatoxins attract monocytes and PMNs on the endothelium. The high mobility group box protein (HMGB) is one of the most studied "alarmin." HMBG is a protein molecule derived from the nucleus of damaged cells [15, 24]. It is released by activated myeloid cells (e.g., neutrophils) [20], macrophages, dendritic cells [25–27], or necrotic cells [26] and acts as a chemoattractant for monocytes, macrophages, dendritic cells, neutrophils, and ϒδ cells [3]. It also participates to the secretion of pro-inflammatory cytokines [28] and mediates the monocyte-endothelial interaction by increasing vascular leakage [24, 29]. Fragments of DNA and histones are other well-known potent "alarmins." They originate from damaged tissues and microbial digestion by resident tissue macrophages or activated neutrophils. Peptides and mitochondrial DNA are vigorous alert molecules probably because of their vestigial origin from intracellular bacteria [3].

2.2.2 Pro-inflammatory Phospholipase Pathway

In addition to "alarmins," the release of phospholipids by damaged cell membranes (cellular hypoxia and trauma) or exogenous lipopolysaccharides (e.g., LPS-endotoxin) and polymers (lipoteichoic acid and peptidoglycans) alert the innate immune system by activating the complement and the contact phase proteins system (FXII, kallikrein, and kininogen). Phospholipids activate the phospholipases A_2 and C [30] with the production of arachidonic acid metabolites as leukotriene B_4, prostaglandin E_2, and thromboxane A_2 [31]. The activation pathway of phospholipase A_2 and C is detailed in Fig. 2.4.

In addition, mast cells release histamine and bradykinin with resulting vasodilation and increased capillary permeability and edema [32]. Just 20–30 min after trauma or microbial invasion, the innate immune cells become activated, Fig. 2.5.

2.2.3 Innate Cellular Immune Defense

The first line of the innate immune defense is represented by PMNs, mostly neutrophils, and monocytes. PMNs are chemoattracted by locally produced cytokines (e.g., TNF-α), leukotrienes, platelet-activating factor (PAF), and complement fragments (c5a) [33–36]. These inflammatory mediators also activate PMNs to express adhesion surface molecules for appropriate ligands on the activated endothelium [37]. This receptor-ligand interaction allows for adhesion of leukocytes to the capillary wall. Thereafter PMNs migrate through the endothelial barrier into the tissues by opportune signaling receptors on the inner surface of the endothelium. In the meanwhile, resident macrophages secrete cytokines (TNFα and IL-1) and chemokines (IL-8) which help the immune and inflammatory cells in self-regulating and crosstalking each other.

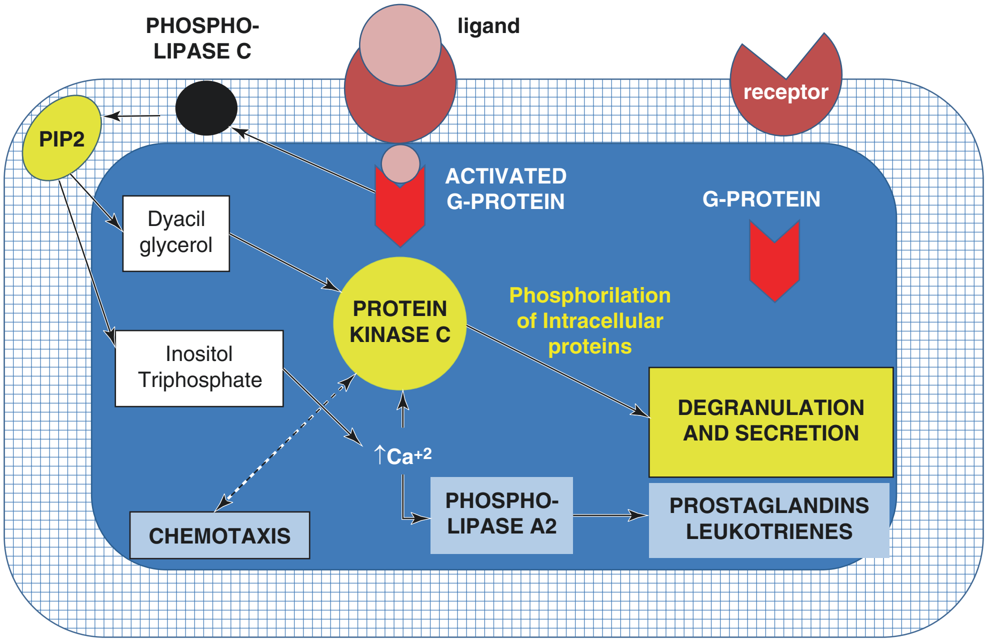

Fig. 2.4 Metabolic pathways of phospholipase A_2 and C. After ligand binding to the appropriate receptor, G protein is activated, this in turn activating the membrane phospholipase C to cleave phosphatidylinositol (PIP2) into diacylglycerol (DAG) and inositol triphosphate. DAG subsequently activates protein kinase C to promote phosphorylation of intracellular proteins that in turn leads leukocytes to degranulate and secrete proteases and other toxic substances. Conversely inositol triphosphate induces the mobilization of calcium ions from storage pools with subsequent activation of phospholipase A_2 by a Ca^{2+}-dependent mechanism. Phospholipase A_2 catalyzes the synthesis of prostaglandins and leukotrienes by arachidonic acid

Fig. 2.5 Main humoral and cellular steps of the hyperinflammatory immune response