DOI: 10.1259/bjr/81696672

Medical management of patients with multiple organ dysfunction arising from acute radiation syndrome

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Abstract. The growing risk of accidental and intentional radiation exposure mandates an examination of our current understanding and management of a significant radiation injury. A considerable number of those patients sustaining a significant body exposure will require treatment in an intensive care unit (ICU). This review examines the complex medical management of acute radiation syndrome and the potential role of modern intensive supportive care measures in patients suffering from subsequent multiple organ dysfunction syndrome. As with most radiation preparedness planning, the resource expenditures in the ICU are scenario-driven. In particular, a mass casualty scenario mandates early estimation of prognosis in order to direct resources to patients who are most likely to have a survivable radiation exposure at the time of ICU admission.

Introduction

The unique characteristics of acute radiation injury and the potential risk of accidental or intentional radiation exposure mandate preparedness planning and education of all personnel who would be involved in the care of patients suffering from acute radiation syndrome (ARS). A previously held international consensus conference addressed the concept of systematically documenting multisystem damage in patients suffering ARS using response categories [1]. This system is very useful to the clinician in the management of a small-volume radiation event, although it may be impractical in a large casualty scenario. As such, planning for such circumstances should be scenario-driven, as the magnitude of an event and the medical resource availability dictate the degree of support possible for a given number of casualties.

Whilst aggressive support is feasible after a small-scale radiation accident, which would likely be associated with few casualties (<100), an improvised nuclear device detonation, where casualties would be >100, and likely in the thousands, warrants a triage algorithm that distributes resources more judiciously. The initial response [2] and medical management guidelines [3] for patients who have been exposed to radiation have recently been reviewed. This paper focuses on the intensive care unit (ICU) management of the critically ill ARS patient.

A significant number of patients will likely require ICU care at some time during their ''manifest phase'', that is the time after exposure in which symptoms become readily apparent. Unfortunately, a prognostic model for this setting does not exist, and as such, clinicians will be faced with the role of discerning those patients with survivable injuries who may require use of scarce ICU resources from those with little or no chance of survival. In this context, it is important to note from the outset that a whole body or significant partial body radiation dose exposure of >10 Gy is uniformly lethal; comfort care should be employed in these instances.

A comprehensive, structured approach is mandatory in optimising ICU treatment of the patient who manifests ARS and its complications. Successful administration of intensive care is dependent upon three conditions: (i) the radiation-induced damage to haematopoietic stem cells is reversible; (ii) the other (non-haematopoietic) injuries are survivable; and (iii) sufficient medical resources are available as patients become critically ill.

Management of multiple organ dysfunction syndrome (MODS) after radiation injury

The term multiple organ dysfunction syndrome (MODS) was established by an expert consensus conference to describe the ''continuum of physiologic derangements'' and subsequent dynamic alteration of organ function that may occur during acute illness [4]. Protracted derangement of homeostatic mechanisms responsible for maintaining organ function will eventually lead to frank organ failure; if widespread, this may culminate in multiple organ system failure (MOSF) [4]. Irradiated victims may present with MODS early (with supralethal exposure), during the manifest phase (as neutropenia and infections evolve) or late (as organ failure ensues from depletion of stem cells responsible for renewal).

For the following discussion of specific organ systems, principles of resource supply and realistic patient triage apply. Some assessment of radiation exposure dose is imperative in directing resources to patients who are most likely to have both a survivable injury and the lowest likelihood of frank MOSF at the time of ICU admission.

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The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the US Army or the Department of Defense.

Neurological

The patient who manifests the neurovascular subsyndrome of ARS has suffered a lethal injury and is usually triaged expectantly [5]. However, causes of altered mental status in the ICU are multitudinous, and include metabolic, hepatic, uraemic and septic encephalopathies, delirium, medication effects, structural disorders, electrolyte disturbances, hypoxaemia, hypercapnia and hyperglycaemia, among others. Accordingly, an accurate assessment of radiation exposure dose is imperative in streamlining the approach to the patient with neurological dysfunction. It must be emphasised that early endotracheal intubation should be performed if depressed consciousness threatens to impair gas exchange or allow for aspiration. Use of parenteral analgesics should be extremely liberal, with judicious adjunctive use of anxiolytics and sedatives as clinically warranted in those patients who are intubated [6]. In addition, in the patient who requires mechanical ventilation, use of a protocol that includes daily sedative interruption and patient assessment is recommended, as this intervention has been shown to decrease length of ICU stay, duration of mechanical ventilation, sedation dose, and the need for diagnostic studies for evaluation of mental status changes [7].

Cardiovascular

Preventing or limiting MODS requires sufficient end-organ perfusion. Accordingly, early ARS, which is manifested by a profound pro-inflammatory state and extensive systemic capillary leak [8] consistent with systemic inflammatory response syndrome, should be approached with liberal use of crystalloid and colloid solutions and blood products as indicated. Assumption of distributive or hypovolaemic shock in the hypotensive ICU patient who has entered the ''manifest illness'' phase after sustaining a radiation exposure or combined injury is a reasonable starting point, as prolonged hypoperfusion (regardless of cause) may initiate MODS. In addition, hyperpyrexia, cutaneous burn injury, vomiting and diarrhoea may contribute significantly to electrolyte and fluid losses. These losses may be underestimated and mandate adequate repletion. Meticulous attention to clinical parameters, including skin turgor and moisture, sensorium, blood pressure, heart rate, urine output and relevant laboratory indices, is essential to guiding volume resuscitation initially [9]. However, invasive haemodynamic monitoring that includes prudent use of arterial and central venous access should be utilised when necessary. Aggressive fluid administration is indicated in the patient with distributive shock physiology, haemorrhage following trauma, or evolving ARS. Conversely, careful fluid restriction should be applied in the patient with coincident acute respiratory distress syndrome (ARDS) [10] or established hepatic veno-occlusive disease [11]. Clinical situations may dictate simple use of jugular venous pressure measurements and waveforms, or may mandate pulmonary artery catheter placement. In addition, the ARS patient with refractory hypotension or hypoperfusion may require vasopressors or inotropes. Choice of agent depends on many variables, including underlying co-morbidities, causative aetiology and desired effects. The reader is referred to reviews that address the intricacies of such management [12–14].

Pulmonary

The patient with ARS may exhibit specific acute pulmonary manifestations that are particularly unique to their exposure history, occur in immunosuppressed or post-transplant populations irrespective of aetiology, or occur in all patients with progressive MODS that includes lung dysfunction. The first category includes acute radiation pneumonitis, and inhalation and contamination injury; the second includes idiopathic pneumonia syndrome, diffuse alveolar haemorrhage (DAH) and neutrophil-induced pulmonary toxicity; the third includes acute lung injury (ALI) or ARDS. The pathogenesis of lung injury is primarily mediated by cellular activation, immune mechanisms and various chemokines, including transforming growth factor-β, interferon-γ, tumour necrosis factor-α, and interleukin-1β (IL-1β) and IL-10 [15].

The exudative lung injury that occurs acutely after radiation exposure has been well described, and pro-inflammatory cytokines are thought to be central to its pathogenesis [16, 17]. Corticosteroids represent the cornerstone of current treatment, although there are experimental data suggesting a role for specific cytokine therapy [18]. No airway decontamination is necessary in the setting of a pure radiation exposure; however, decontamination measures that include pulmonary lavage may be useful if inhalation of radioactive particles or sediment is suspected [19]. In addition, early bronchoscopy may be useful in assessing for non-specific inhalation airway injury (*i.e.* burn or thermal) [20]. Therapeutic bronchoalveolar lavage may have a role in established injury [21].

Idiopathic pneumonia syndrome (IPS) is a heterogeneous non-infectious interstitial or alveolar pneumonitis following bone marrow transplantation, with a described incidence of approximately 12% [22]. IPS is associated with total body irradiation (TBI) regimens, occurs at a median 22 days after transplant (range 4–106 days), and has a 75% mortality despite aggressive support. There is a broad spectrum of morbidity that arises in the subacute post-transplant period, ranging from incidentally noted infiltrates to frank ARDS, and attributable mortality from progressive respiratory failure may be as high as 32% [22]. Treatment is primarily supportive.

DAH is another non-infectious pulmonary syndrome that is seen not uncommonly in the early post-transplant period following haematopoietic stem cell infusion. Whilst white blood cell recovery and TBI are associated with development of this complication, uses of granulocyte colony-stimulating factor (G-CSF) and peripheral blood stem cell source for transplant are not [23]. Pre-transplant TBI has been speculated to initiate the lung injury that eventually evolves into DAH [23], a theory of particular import in the context of ARS management after significant source exposure. Supportive therapy that ensures gas exchange and limits bleeding is the cornerstone of management, although high dose systemic corticosteroids have been administered with some success [24].

There is concern that neutrophil recovery following marrow transplantation (''peri-engraftment respiratory distress syndrome'') and/or administration of G-CSF

used to hasten neutrophil recovery may precipitate or worsen ALI [25]. Pulmonary sequelae of G-CSF are often transient and include cough, dyspnoea, and interstitial or alveolar infiltrates, but in the setting of prior lung injury or co-administration with other therapeutic agents, significant toxicity may occur. In addition, full-blown ARDS has been described after isolated G-CSF administration [26]. The widespread prescription of G-CSF that would accompany large numbers of radiation casualties would undoubtedly increase the incidence of related pulmonary sequelae. Accordingly, careful monitoring and judicious use of G-CSF should be emphasised in the patient at risk. However, in a recent Phase II trial of patients with severe sepsis and lung dysfunction [27], G-CSF improved gas exchange and surrogate markers of lung inflammation and was not associated with worsened ARDS or MODS.

Patients with a non-specific pattern of acute lung dysfunction that meet certain criteria are defined as having ALI or ARDS based on the severity of hypoxaemia [28]. Regardless of the insult that precipitates ALI or ARDS in the patient with ARS, management includes judicious fluid administration and avoidance of iatrogenic lung injury. Whilst initial therapeutic measures may include the selective use of non-invasive positive pressure ventilation [29, 30], the majority of ARS patients who manifest evolving MODS are likely to require endotracheal intubation and subsequent prolonged ventilator support. Experimental [31] and clinical observations have led to the realisation that indiscriminate application of the ventilator itself may worsen lung injury, through complex mechanical and biological processes that induce a pro-inflammatory cellular response mediated by cytokines and other factors [32]. The landmark Acute Respiratory Distress Syndrome Network (ARDSNet) trial [33] showed a mortality benefit, a reduction in days with non-pulmonary organ system failure, a reduction in ventilator-free days and a reduction in pro-inflammatory plasma cytokine levels (IL-6) from a lung-protective ventilation strategy that utilized low tidal volumes ($6\ cm^3\ kg^{-1}$) and limited airway pressures. These benefits were independent of measured lung compliance or injury precipitant (trauma, sepsis, pneumonia, etc.). in addition, ARDSNet revealed that while initial hypoxaemia is often used as a surrogate for degree of lung injury, it is not predictive of subsequent mortality. While the reasons for these findings have been extensively debated [34], use of a protective ventilatory strategy that limits airway pressures and inspired oxygen fraction, optimises organ perfusion and allows for permissive hypercapnia (if not otherwise contraindicated) appears to be indicated in limiting MODS and improving outcomes [35]. In addition, there may be a role for corticosteroids in ARS, as both in the intermediate phase of radiation lung injury and in established ARDS, pathology reveals fibroproliferative modelling [17, 36].

Lastly, it must be emphasised that use of mechanical ventilation in patients with ARDS after ARS (or marrow transplantation performed to support it) should be applied commensurate with available resources and outcomes data [37, 38]. Non-invasive ventilation may provide an alternative means of support [39–41], which may be associated with lower morbidity and mortality in certain instances [39].

Gastrointestinal

The gastrointestinal (GI) tract is inherently sensitive to radiation given its high cell turnover; the entire mucosal layer is completely renovated in 72 h [42]. After receiving whole body or significant partial body radiation exposures of >5 Gy, GI complications can occur rapidly. Patients may present with nausea, vomiting, stomatitis, abdominal bloating, ileus, diarrhoea or bloody stools [42]. This may be complicated by sepsis, volume depletion and shock due to electrolyte imbalance or haemorrhage.

Splanchnic hypoperfusion and gut mucosal injury have been theorized as central components in the development of MODS [43]. Importantly, the early loss of GI integrity and distributive hypotension seen in critically ill ARS patients with significant exposure may expedite this process [42, 44]. Whether the actual inciting event leading ultimately to MODS involves reperfusion injury, free radical formation, actual bacterial translocation or some other mechanism is a matter of debate [42, 43, 45]. However, regardless of the specific pathophysiology, some general management principles are important in preserving the integrity of the GI tract.

Selective digestive decontamination (SDD), *i.e.* the use of antimicrobial therapy to reduce colonization by potentially pathogenic micro-organisms in the gut flora, has been shown to lower nosocomial infection and to improve ICU survival [46–49]. SDD has been used [50] in patients with ARS with apparent benefit, and implementation of this strategy should be strongly considered [42, 50].

Pharmacological stress ulcer prophylaxis should be instituted early with sucralfate, H2 blockers or proton pump inhibitors [51], as bleeding and loss of mucosal integrity from the GI subsyndrome is to be expected [8, 42, 50, 52]. Nutritional support with enteral feeding is best if possible, although use of total parenteral nutrition may be necessary [53, 54]. Emesis, diarrhoea and motility disturbances are common and should be treated aggressively [53].

Liver-associated enzyme abnormalities are a non-specific indicator of injury in the patient with evolving MODS. They may herald either biliary or hepatic dysfunction, and ARS-related diagnostic considerations include hepatic veno-occlusive disease [11], acalculous cholecystitis [55], graft-versus-host disease (GVHD), cholestasis lenta and drug-induced hepatotoxicity [56].

Skin

The skin may be injured from thermal burns or burns that may arise after radiation. Extensive burn injury may lead to immunosuppression through altered neutrophil activity, T-lymphocyte dysfunction and dysregulation of cytokines, and often results in significant increase in mortality [52]. Granulocytes are important elements of the host response after thermal burn and infection. Impairment in bone marrow granulopoiesis after thermal injury results in decreased neutrophil chemotaxis [57] and bactericidal activity [58], and alterations in the production of G-CSF [59]. A recent study found impaired granulopoiesis after thermal burns, which may be related to hyporesponsiveness to G-CSF rather than defective endogenous G-CSF production [60]. Such a finding could significantly impact the management of patients

with combined radiation injury and thermal burns. After sustaining a threshold dose of whole body radiation, G-CSF becomes an integral part of post-exposure management. It is unclear whether increased dosing of G-CSF is beneficial.

Infectious disease

Infection is a significant contributor of mortality in victims of ARS [61]. In non-neutropenic patients, antibiotics should be directed towards the foci of infection and the most likely pathogens. For those who experience significant neutropenia (absolute neutrophil count (ANC) $<500\ \mu l^{-1}$), broad spectrum prophylactic antimicrobials should be employed. Such prophylaxis should include a fluoroquinolone (FQ) with streptococcal coverage (with penicillin or amoxicillin if not inherently covered by the FQ), an antiviral agent if the patient is seropositive for herpes simplex virus, and an antifungal agent. These recommendations and their rationale are published elsewhere [3].

Prophylactic antimicrobials should continue until the patient experiences a neutropenic fever (and requires initiation of empiric treatment with parenteral antimicrobials) or neutrophil recovery (ANC $>500\ \mu l^{-1}$). In patients who experience an initial fever, FQ should be stopped and therapy with parenteral antibiotics that cover Gram-negative bacteria (in particular *Pseudomonas aeruginosa*) should be initiated, given the virulent nature of such infections. Therapy of patients with febrile neutropenia should follow the guidelines published by the Infectious Diseases Society of America [62].

Recombinant human activated protein C (drotrecogin alfa) represents a significant advance in patients with severe sepsis, resulting in mitigation of MODS-precipitating inflammatory and thrombotic components of the body's response to severe infection [63]. However, drug cost and infeasibility of administration in patients with evolving marrow failure, and increased propensity for bleeding would likely limit its use for ARS-associated MODS, particularly in a mass casualty situation. Consideration in a small-casualty scenario in patients experiencing early onset MODS less than 48 h after exposure may be reasonable, but there are no published trials to define its role in victims of ARS.

Renal

Early renal dysfunction secondary to ARS is likely prerenal in origin, given the tissue hypoperfusion commonly seen after significant exposure. Direct radiation nephropathy is usually a chronic concern [64]; however, renal insufficiency is a common phenomenon in the ICU [65]. Application of renal replacement therapy or dialysis can be pursued [66], but resource limitations may limit widespread application.

Endocrine

The importance of the endocrine system in helping to orchestrate the body's response to critical illness has been increasingly recognised [67]. Injury to the thyroid following radiation exposure has been well described [68]; true hypothyroidism should be treated, although sick euthyroid syndrome must be considered [69].

Strict glycaemic control should be considered a fundamental part of ICU management. In a study of mechanically ventilated surgical ICU patients, use of an intensive insulin regimen (maintenance of blood glucose between 80–110 mg dl^{-1}) was associated with a statistically significant reduction in ICU mortality, in-hospital mortality, number of bloodstream infections, need for mechanical ventilation, episodes of acute renal failure requiring renal replacement therapy, incidence of critical illness polyneuropathy, non-specific markers of inflammation, and the median number of red cell transfusions [70]. Intriguingly, the greatest reduction in mortality was seen in those patients who manifested MOSF with a proven septic focus. In addition, strict glycaemic control is associated with improved wound healing [71] and has an established therapeutic role in attenuating the hypermetabolic response to burn injury [72]. These effects are of particular benefit to the patient with ARS who manifests MODS, who may require extensive early surgery, may be profoundly leukopenic, may have an injured integumentary system from burn or traumatic injury, and may have endothelial dysfunction. The deleterious immunosuppression and unchecked pro-inflammatory response associated with each of these factors may be considerably mitigated by intensive insulin therapy and strict glycaemic control.

Occult relative adrenal insufficiency is being increasingly recognised as a cause of morbidity in the critically ill [73, 74]. Corticosteroids may have several indications for use in ARS, including DAH and ALI [24, 36], dermatological injury from ARS, GVHD, post-transplant immunosuppression and septic shock [75]. In sepsis, steroid replacement therapy has been associated with decreased mortality, as well as a decreased pressor requirement [74, 75]. Assessment of adrenal function may also have prognostic significance [76].

Haematological

Because the lymphohaematopoietic elements are exquisitely radiosensitive, cytopenias are likely to be commonplace in any patient with a >2 Gy exposure. Subpopulations of selectively radioresistant stem cells and/or accessory cells exist and may contribute to haematopoietic reconstitution with exposure up to 6 Gy [77, 78]. The resultant haematological crisis ensues over 1–4 weeks, with more rapid onset at higher doses. The attendant lymphopenia, bone marrow atrophy, pancytopenia and clinical sequelae (infection, bleeding and poor wound healing) contribute to the mortality of ARS and accordingly, protracted administration of haematopoietic colony-stimulating factors (CSFs), blood product support and antibiotics will be required. Patients with burns and/or wounds will likely be at higher risk for poor wound healing, bleeding and infection due to lymphohaematopoietic suppression [79]. Moreover, these injuries contribute synergistically to the lethality of patients with haematopoietic syndrome, lowering the $LD_{50/60}$.

Sparing of bone marrow precursors may also occur given the likelihood of inhomogeneous exposures. This may allow for eventual reconstitution of haematopoiesis, and allow for survival if the dose to other organs is not too great.

Table 1. Guidelines for treatment of radiation victims [3, 98]
(a) Small-volume scenario (<100 casualties)

	Proposed dose range (Gy) for cytokines	Proposed dose range (Gy) for antibiotics[c]	Proposed dose range (Gy) for referral for SCT consideration
Healthy individual, no other injuries	3–10[a]	2–10[d] (and ANC <500 μl^{-1})	7–10 (for allogeneic SCT); 4–10 (if previous autograft stored or syngeneic donor available)
Multiple injuries and/or burns	2–6[a]	2–6[d] (and ANC <500 μl^{-1})	N/A

(b) Mass casualty scenario (>100 casualties)

	Proposed dose range (Gy) for cytokines	Proposed dose range (Gy) for antibiotics and other supportive care[c]	Proposed dose range (Gy) for referral for SCT consideration
Healthy individual, no other injuries	3–7[a]	2–7[d]	7–10 (for allogeneic SCT)[b]; 4–10 (if previous autograft stored or syngeneic donor available)[b]
Multiple injuries and/or burns	2–6[b]	2–6[b,d]	N/A

Consensus guidance for treatment is based on threshold whole body or significant partial body exposure doses. Events due to a radiation accident or detonation of a radiation dispersal device resulting in <100 casualties, and those due to detonation of an improvised nuclear device resulting in >100 casualties have been considered.

[a]Consider initiating at lower exposure in non-adolescent children and the elderly. Initiate G-CSF or GM-CSF treatment in those victims who develop an ANC <500 μl^{-1} and who are not already receiving a CSF.

[b]If resources available.

[c]Prophylactic antibiotics include fluroquinolone, acyclovir (if seropositive for HSV or past medical history of HSV) and fluconazole when ANC <500 μl^{-1}.

[d]ANC <500 μl^{-1}. Antibiotics should be continued until neutrophil recovery has occurred. Follow Infectious Diseases Society of America guidelines [62] for febrile neutropenia if fever develops while on prophylaxis.

N/A, not applicable (due to poor outcome); SCT, stem cell transplantation; G-CSF, granulocyte colony-stimulating factor; GM-CSF, granulocyte-macrophage colony-stimulating factor; ANC, absolute neutrophil count; HSV, herpes simplex virus.

Blood product support will be required for patients with traumatic injuries and those with severe bone marrow damage resulting from radiation-induced aplasia. Fortunately, the latter complication does not typically occur before 2–4 weeks, during which time blood donors may be rapidly identified. Several series suggest that anaemia is well tolerated in critically ill patients and that transfusions have deleterious effects. These effects include immunomodulatory [80] and immunosuppressant effects, which may contribute to nosocomial [81] and transfusion-related infections [82]. Moreover, several series have demonstrated the safety (if not superiority) of using a 7 g dl^{-1} transfusion threshold, with the goal of maintaining a haemoglobin level of 7–9 g dl^{-1} [83].

All cellular products should be leukoreduced and irradiated (2500 cGy) to prevent transfusion-associated GVHD. Leukoreduction should be performed to lessen febrile non-haemolytic reactions and to avoid the immunosuppressive effects of blood transfusion [84, 85]. Moreover, leukoreduction affords some protection against platelet alloimmunisation and protection against acquiring cytomegalovirus infections [86]. In sum, life-saving blood products should not be withheld but should be leukoreduced and irradiated whenever possible.

Haematopoietic CSFs should be implemented in patients subjected to acute high dose radiation (Tables 1 and 2) [3].

Because of concerns surrounding blood transfusion therapy in ICU patients, erythropoietin as a transfusion-sparing cytokine has been investigated. In a randomised trial of heterogeneous ICU patients, recombinant human erythropoietin was shown to reduce the number of allogeneic red blood cell transfusions [87]. Unfortunately, however, trials examining administration in patients after bone marrow transplantation have been less encouraging [88, 89], and the profundity of marrow injury likely to be seen after significant radiation exposure may limit the efficacy of erythropoietin.

Disseminated intravascular coagulation (DIC) is an acquired disorder of widespread coagulation, which may manifest clinically with either bleeding or thrombosis [90]. Those conditions associated with DIC (*i.e.* trauma, sepsis, transfusion reaction, endothelial injury) may coexist in the ARS patient, and the microvascular thrombotic phenomena arising from DIC are a speculated pathogenic mechanism in initiation of MODS. Treatment is primarily supportive; judicious use of blood product support, anticoagulants, antifibrinolytics and recombinant human activated protein C may be indicated.

Venous access and thromboembolic prophylaxis

Whilst peripheral access should be obtained and used preferentially, the ARS patient with MODS will almost certainly require central venous access for invasive haemodynamic monitoring or for administration of vasoactive medications or parenteral nutrition. Interventions that have been shown to reduce the incidence of catheter-related bloodstream infections include the implementation of barrier protections during

Table 2. Recommended doses of cytokines [3]

Cytokine	Adults	Paediatrics	Pregnancy[a]	Precautions
G-CSF or filgrastim	5 μg kg^{-1} per day SC, and continued until ANC >1000 μl^{-1}	5 μg kg^{-1} per day SC, and continued until ANC >1000 μl^{-1}	Class C[b] (same as adults)	Sickle cell haemoglobinopathies, significant coronary artery disease, ARDS. Consider discontinuation if pulmonary infiltrates develop at neutrophil recovery
Pegylated G-GSF or pegfilgrastim	6 mg, SC × 1 dose	For adolescent >45 kg: 6 mg, SC × 1 dose		
GM-CSF or sargramostim	250 μg m^{-2} per day, SC, and continued until ANC >1000 μl^{-1}	250 μg m^{-2} per day, SC, and continued until ANC >1000 μl^{-1}		

[a]Experts in biodosimetry must be consulted. Any pregnant patient with exposure to radiation should be evaluated by a health physicist and maternal–fetal specialist for an assessment of risk to the fetus.
[b]Class C, refers to US Federal Drug Administration Pregnancy Category C; studies have shown animal, teratogenic and/or embryocidal effects but there are no controlled studies in animals or women.
G-CSF, granulocyte colony-stimulating factor; GM-CSF, granulocyte-macrophage colony-stimulating factor; SC, subcutaneous; ANC, absolute neutrophil count; ARDS, acute respiratory distress syndrome.

insertion [91] and the use of antibiotic-impregnated catheters [92, 93]; in addition, insertion sites free of denuded or burned integument should be utilised if possible [94, 95]. A recent review [96] details insertion technique and the prevention of associated complications.

Prophylaxis aimed at prevention of venous thromboembolism should be implemented uniformly, with specific attention to risk factors and potential for bleeding [97].

Conclusions

Management of the critically ill patient with ARS requires a systematic, multidisciplinary approach that emphasises proactive interventions and attention to detail. Despite considerable advances in ICU care, it is probable that survival of a patient with radiation injury will ultimately be limited by the number of casualties and the finite availability of medical resources. Accurate biological and clinical indicators are needed so that patients can be appropriately triaged.

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