ICM on Open Injuries - Submission of the consensus recommendation

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RQ: In farmyard-related open injuries, should empirical antibiotic regimens include antifungal agents in addition to anaerobic coverage?

Section 1: Background

Farmyard-related open injuries represent a unique and high-risk category of trauma with an inherently contaminated wound environment. Soil harbors vast numbers of aerobic, anaerobic, and fungal microorganisms, with bacteria and actinomycetes forming the largest fraction of the soil's microbial population. Farm machinery is the most common mechanism, accounting for 34.8–44.9% of non-fatal farmyard injuries in major epidemiological studies [1].

Standard antibiotic management of open fractures targets gram-positive and gram-negative bacteria, with the addition of anaerobic coverage (penicillin or ampicillin) specifically recommended for farmyard injuries, given the risk of clostridial myonecrosis. A prospective study by Wynn et al. [2] confirmed that anaerobic infections occur in 44% of deep infections in agricultural open fractures, significantly higher than in non-agricultural trauma (9.1%).

However, fungal infection following traumatic wounds is an under-recognized but documented complication. Invasive fungal infections (IFIs) have been reported after motor vehicle crashes, agricultural accidents, blast trauma, and natural disasters. Ali et al. [3] documented that fungal organisms (Candida, Aspergillus, Absidia/Mucor, Fusarium, Trichosporon, and others) were isolated from 8 out of 26 deep wound infections following open agricultural upper-extremity injuries. Trauma-related IFIs carry mortality rates as high as 40% in civilian literature [3].

The key unresolved clinical question is whether routine empirical antifungal therapy is justified in all farmyard open injuries at presentation, or whether it should be reserved for specific high-risk presentations based on wound characteristics (necrosis, failure of antibacterial therapy). Currently, no prospective randomized trial addresses this question specifically for farmyard civilian trauma.

Section 2: Data extraction table

S.no	Author, year of publication, Country	Study Design	Sample Size (add individually for each group if multiple groups compared)	Study population (Inclusion and exclusion criteria)	Groups compared	Results
1	Zalavras et al., 2005, USA[4]	Narrative review / Expert opinion	N/A	Open fractures, all Gustilo types	Antibiotic regimens by fracture type	Infection risk: 0–2% Type I; 2–10% Type II; 10–50% Type III; Cephalosporin + aminoglycoside standard; Penicillin/ampicillin added for anaerobic coverage in farmyard injuries; Recommended duration 3 days + 3 more for subsequent procedures; No fungal coverage addressed.
2	Angoules et al., 2007,UK[1]	Narrative review	N/A (review of multiple datasets)	Farmyard injuries	Farmyard injuries vs. general industrial injuries	Farmyard wounds are a priori contaminated with anaerobic organisms and always carry the risk of clostridial myonecrosis; cephalosporin + gentamicin + penicillin/ampicillin recommended; no antifungal recommendation made; fungal coverage not addressed.
3	Ali et al., 2008, USA[3]	Retrospective review	214	Open agricultural upper extremity injuries, Jan 1992–	Type 1 vs. Type 2 vs. Type 3 upper extremity	40/214 (18.7%) developed clinical infection; 7/26 surgically managed infections had fungal. No patient had a fungal infection in

				Dec 2002, Level 1 Midwest hospital. Exclusion: no open wound, refused consent	agricultural injuries	isolation from bacteria. The author states: insufficient data to recommend empirical antifungal therapy routinely; recommend high suspicion + fungal cultures + pathology + empirical antifungal based on gross wound appearance, tissue hypoxia, diabetes, steroids.
4	Obradović-Tomašev M. et al., 2016, Serbia[5]	Retrospective cross-sectional study	n = 60 corn picker hand injury patients; comparison group n = 644 other hand injury patients	Patients treated for severe corn picker hand injuries at the Clinic of Plastic and Reconstructive Surgery, Clinical Centre of Vojvodina, 2006–2012. Age: 95% between 21–59 years; 88.3% male. Exclusion: none specified. All had no increased risk factors for fungal infection (immunocompetent)	Corn picker injuries vs. other hand injuries (circular saw group as comparator for fungal incidence)	Fungal infection in **9/60 (15%)** of corn picker patients vs. **1/644 (0.16%)** of other hand injuries. *Aspergillus* spp. in 7 patients, *Candida* spp. in 3, *Mucor* spp. in 1; one patient had all three simultaneously. All infections co-occurred with bacterial growth (*S. aureus* + *Enterococcus* spp. in all cases); fungal infection appeared ≥7 days post-injury with graft loss and tissue necrosis. Antibiotic prophylaxis discontinued upon clinical suspicion; treatment: systemic + topical antifungals (amphotericin B, voriconazole, fluconazole, miconazole, nystatin) + repeated surgical debridement **No reamputation required** in any patient Culture sensitivity for mucormycosis is only 30% — repeated biopsy/histopathology is essential.
5	Ganesan et al., 2019, USA[6]	Observational cohort	246 soldiers, 413 wounds	US service members injured in Afghanistan, June 2009–Dec 2014, with laboratory evidence of fungal infection. Inclusion:	IFI (n=94, 143 wounds) vs. High-suspicion (n=61) vs. Low-suspicion (n=91)	Wounds without necrosis and without localized signs/symptoms of infection do NOT require immediate antifungal therapy. Wounds with persistent necrosis after ≥2 debridements = IFI. So, Empirical antifungal use.

				penetrating wounds with operative cultures/histopathology		Blast injury only — limited direct applicability to farmyard injuries.
6	Tribble et al., 2020, USA[7]	Narrative review (military trauma literature)	N/A (multiple sub-studies pooled)	US combat casualties with IFI; open blast wounds contaminated with soil/organic debris	IFI vs. IFI- High-suspicion vs. IFI-Low-suspicion	Dual antifungal therapy (liposomal amphotericin B + broad-spectrum triazole e.g., voriconazole or posaconazole) is recommended when IFI is strongly suspected. Co-infection with bacteria is common: vancomycin + meropenem is recommended. No civilian farmyard-specific data
7	Mucci N. et al., 2020, Italy[8]	Systematic review	53 articles included [3 narrative reviews, 50 original articles] (35 cross-sectional studies, 11 case series, 2 case reports, 1 cohort, 1 case-control)	Agricultural workers with upper limb injuries; all ages, multiple countries. Exclusion: non-agricultural jobs, chronic occupational diseases, studies concerning only children/adolescents, editorials without quantitative data	N/A	Upper limb injuries account for ~1/3 of all agricultural accidents; hand is the most affected body part (20.5%) Predominant injury type: open wounds, lacerations, fractures, amputations; machinery (tractors, corn pickers, grain augers, hay balers, power take-offs) is the leading cause Irrigation + surgical debridement + tetanus + antibiotic prophylaxis recommended in management **No Evidence found on antifungal use in agricultural trauma**, which is a significant evidence gap.
8	Wynn et al., 2022, USA[2]	Retrospective cohort	178 (89 agricultural, 89 non-agricultural)	Open lower extremity fractures	Agricultural vs non-agricultural trauma	Deep infection rate 21% vs 10%. Anaerobes in 44% of agricultural infections (Enterococcus, Pseudomonas, Clostridium

						perfringens). Strong support for anaerobic prophylaxis. No fungal data reported.

Section 3: Results summary

Six studies were included in this review addressing antibiotic/antifungal management in farmyard-related open injuries. The evidence base is predominantly composed of retrospective cohort studies, narrative reviews, and military-derived observational data. No prospective randomized trial directly addresses empirical antifungal use in civilian farmyard open fractures.

Regarding bacterial infection burden: Wynn et al. (2022)[2] provided the strongest evidence confirming that agricultural open fractures carry a significantly higher deep infection rate (21%) compared to non-agricultural controls (10%), with anaerobic organisms accounting for 44% of infections in the agricultural group versus 9.1% in controls. The most common anaerobes were Enterococcus sp., Pseudomonas aeruginosa, and Clostridium perfringens. This data robustly supports the addition of anaerobic antibiotic coverage (penicillin/ampicillin) to the standard regimen in farmyard injuries, consistent with expert guidance from Angoules et al.[1] and Zalavras & Patzakis [4].

Regarding fungal infection in agricultural trauma: Ali et al. (2008)[3] provided relevant data for civilian farmyard injuries. Fungal organisms were isolated from 7 of 26 (31%) surgically managed wound infections following open upper-extremity agricultural injuries. The identified fungi included Candida sp., Aspergillus sp., Absidia/Mucor sp., Fusarium sp., Trichosporon sp., Acremonium sp., Penicillium sp., and Sporobolomyces sp., a notably diverse profile. Critically, no patient developed a fungal infection without concomitant bacterial growth, and the authors concluded that current data are insufficient to recommend routine empirical antifungal therapy for all agricultural injuries requiring surgical management.

Obradović-Tomašev et al. (2016)[5] provided the most direct civilian evidence, documenting a **15% fungal infection rate specifically in corn picker hand injuries**, compared to only 0.16% in other hand trauma treated at the same center. All fungal infections occurred in immunocompetent patients, reinforcing that host immunodeficiency is **not a prerequisite** for post-traumatic fungal infection in agricultural settings. Importantly, infections presented clinically only after ≥7 days, with graft loss and necrosis as the cardinal signs, and all were treated successfully with targeted antifungal therapy without reamputation.

Regarding IFI classification and antifungal triggers: Ganesan et al. (2019)[6] and Tribble et al. (2020)[7], working primarily with military blast injuries, demonstrated that the key predictor requiring antifungal therapy is **persistent wound necrosis after ≥2 surgical debridements,** combined with laboratory evidence of fungal infection. Wounds lacking necrosis and localized signs of deep soft tissue infection can be safely monitored without antifungal therapy. Mucorales fungi predominated in true IFI wounds (39%) versus low-suspicion wounds (9%), suggesting that fungal speciation is clinically meaningful. When antifungal therapy is indicated, dual therapy with **liposomal amphotericin B plus a broad-spectrum triazole** (voriconazole or posaconazole) is recommended due to the polymicrobial nature of mould infections.

Key gap: All military IFI data derive from blast injuries with massive tissue disruption and large blood transfusions — a fundamentally different physiological context from civilian farmyard trauma. The incidence, risk factors, and optimal management of fungal infections, specifically in civilian farmyard open fractures, remain poorly studied.

Section 4: Discussion

Farmyard open injuries present unique infectious challenges because of their heavily contaminated wound environment, high anaerobic organism burden, and potential for diverse fungal inoculation from soil. The available literature clearly establishes that these wounds require antibiotic coverage beyond the standard gram-positive/gram-negative regimen used for non-agricultural open fractures, particularly including anaerobic coverage.

The role of empirical antifungal therapy is less straightforward and remains a subject of ongoing debate. The evidence from Ali et al.[3] documents fungal organisms in a substantial proportion of surgically managed agricultural wound infections. However, fungal growth consistently occurred alongside bacterial infection rather than in isolation, raising the possibility that fungi detected in these wounds may represent colonization or co-contamination rather than primary pathogens. This distinction — contamination vs. true invasive fungal infection — is central to the antifungal debate and was formally operationalized in the IFI classification framework developed by Ganesan et al.[6] for military blast wounds.

Obradović-Tomašev et al. (2016)[5] provided the most direct and specific civilian evidence on this question, documenting **a 15% fungal infection incidence** in corn picker hand injuries, compared to only 0.16% in non-agricultural hand trauma at the same institution. Crucially, all nine affected patients were immunocompetent — none had diabetes, steroid use, or other predisposing host factors — directly refuting the assumption that post-traumatic agricultural fungal infection requires an immunocompromised host. The organisms identified (Aspergillus spp. in 7 patients, Candida spp. in 3, and Mucor spp. in 1, with one polymicrobial case involving all three) mirror those expected from agricultural soil and decaying plant material and are consistent with the profile described by Ali et al.[3] . The local acidosis and immunosuppression that accompany extensive tissue loss in crush injuries may be sufficient to enable normally saprophytic fungal spores to establish pathogenic invasion in otherwise healthy individuals.

A critical observation from the Obradović-Tomašev series is the **timing** of clinical fungal infection: in most cases, signs appeared **only after seven or more days post-injury**, manifesting as color changes of granulation tissue, skin graft loss, and wound necrosis. No patient demonstrated fungal infection at initial presentation. This temporal pattern argues strongly against routine empirical antifungal therapy at first contact, as the invasive infection is simply not yet established at that stage. It instead supports a protocol of active surveillance — twice-weekly wound swabs with low threshold for biopsy and histopathological confirmation — combined with prompt, targeted antifungal initiation once clinical suspicion arises. The fact that all nine patients were treated successfully without reamputation using this reactive, culture-directed approach further validates this strategy.

The Ganesan/Tribble classification stratifies wounds into IFI, High-Suspicion IFI, and Low-Suspicion IFI based on the presence of persistent necrosis after ≥2 debridements, laboratory evidence of fungal infection, and signs/symptoms of deep soft-tissue infection. This framework elegantly separates patients who truly need antifungal therapy from those who can be safely observed. Applying this logic to civilian farmyard injuries, routine empirical antifungal therapy at initial presentation is not supported by current evidence. Rather, a high index of clinical suspicion combined with systematic wound monitoring is appropriate.

Despite this, there are sound biological grounds for maintaining a heightened level of suspicion in selected farmyard injuries. Soil heavily contaminated with organic matter (e.g., manure, compost, grain) harbors Mucorales spores (Rhizopus, Mucor, Lichtheimia) which are the most virulent post-traumatic mould pathogens. Host risk factors that impair fungal clearance — including diabetes mellitus, immunosuppressive medication, vascular compromise, and local tissue hypoxia from crush injuries — further increase the risk. In these settings, the threshold for obtaining fungal cultures, wound biopsy, and empirical antifungal initiation should be lower. The systematic review by Mucci et al. (2020)[8] confirms that corn pickers, grain augers, hay balers, and power take-off devices are the predominant causes of severe upper limb agricultural injuries, and that infection is a well-recognized downstream complication across multiple countries and study designs. Importantly, Mucci et al. explicitly note that **no direct evidence addressing antifungal prophylaxis or treatment in agricultural trauma was identified among 951 screened references,** a finding that formally confirms the evidence gap underlying this consensus question.

The choice of antifungal agent is important. Liposomal amphotericin B remains the broadest empirical agent, covering Mucorales, most Aspergillus, and Fusarium spp. A broad-spectrum triazole (voriconazole or posaconazole) is added in dual therapy protocols due to the intrinsic resistance of Aspergillus terreus to amphotericin B and the activity of triazoles against Scedosporium species documented in soil/manure-related wound infections. Isavuconazole, a newer water-soluble triazole, offers additional options. In practice, Obradović-Tomašev et al.[5] used a mycogram-directed approach: parenteral amphotericin B, voriconazole, or fluconazole for Aspergillus; amphotericin B followed by voriconazole for mucormycosis; and topical nystatin or miconazole for Candida infections, achieving resolution in all cases without reamputation . This validates that culture-directed, targeted antifungal therapy is effective in the civilian agricultural setting when initiated promptly after clinical diagnosis.

A critical limitation of applying the existing military data to civilian farmyard injuries is the fundamentally different injury mechanism. Military blast injuries involve massive tissue destruction, heavy metallic/organic debris, large-volume blood transfusions causing immunosuppression, and polytrauma — all factors absent or less extreme in typical civilian farm machinery injuries. The civilian data from Ali et al.[3] showed an 18.7% overall clinical infection rate and 31% fungal positivity among infected wounds, but with less severe injuries and without the same systemic physiological insult. This makes routine empirical antifungal therapy even less justifiable as a blanket recommendation in civilian agricultural trauma. The Obradović-Tomašev series[5] reinforces this: despite a 15% fungal infection rate in the most severe subgroup (corn picker injuries), a reactive management strategy with vigilant monitoring was sufficient and effective.

Section 5: Risk of bias of included studies

Study	Risk of Bias
Zalavras & Patzakis, 2005	**HIGH** — Narrative review, expert opinion, no systematic methodology
Angoules et al., 2007	**HIGH** — Narrative review, no systematic methodology, expert opinion
Ali et al., 2008	**MODERATE-HIGH** — Retrospective; only minority had initial fungal cultures; no standard prophylaxis protocol
Obradović-Tomašev et al., 2016	**MODERATE** — retrospective; single center; small sample; no standard antifungal prophylaxis protocol; no control for injury severity between groups.
Ganesan et al., 2019	**MODERATE** — Observational; military blast injuries only; limited civilian applicability; retrospective case definition
Tribble et al., 2020	**MODERATE** — Narrative review of military data; no civilian farmyard data
Mucci et al., 2020	**MODERATE** — systematic review with PRISMA methodology and quality assessment tools applied; however, included studies are predominantly cross-sectional with low-to-intermediate methodological quality; no randomized trials included.
Wynn et al., 2022	**MODERATE** — Retrospective; small sample; control group not matched for injury characteristics (fracture type and severity differed)

Section 5: Response/Recommendation

Empirical antifungal agents should NOT be routinely included in the initial antibiotic regimen for all farmyard-related open injuries.

Section 6: Level/ strength of Evidence:

LOW

Justification: No randomized controlled trial exists addressing empirical antifungal use in farmyard open fractures or agricultural trauma. The available body of evidence remains dominated by retrospective studies, narrative and systematic reviews, and military observational cohort data. The overall body of evidence does not support routine empirical antifungal use but does highlight the need for vigilance and early antifungal initiation when clinical triggers are present.

References:

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