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EDITORIAL

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Report from the 2024 Dorothy Russell Havemeyer Working Group Meeting on Consensus Definitions for Foal Sepsis

The Dorothy Russell Havemeyer Working Group on Consensus Definitions of Foal Sepsis first met in March of 2018. Inclusion in the working group required submission of prospectively collected data on ill foals presented to individual participant's hospitals. The database was extensive and ultimately included over 1000 foals.[1] Specific highlights from the 2018 meeting included:

1. *Age groupings*: The participants agreed that the age groupings of equine neonates previously described were acceptable.[2] The age groups are (A) the Newborn Foal—birth through 3 days of age—and (B) the Neonatal Foal, 4–14 days of age.
2. *Defining sepsis*: The participants agreed, after reviewing multiple studies,[3–14] that equine sepsis be defined as the 'presence of documented or suspected infection combined with the presence of the systemic inflammatory response syndrome (SIRS)'. Additionally, the participants agreed that positive blood culture or single site of infection would not define sepsis without evidence of systemic inflammation, consistent with the sepsis definition in human paediatrics.[12–15]
3. *Defining SIRS*: SIRS was defined as having at least two of four parameters noted in Table 1 outside the normal range, with normal ranges described by age grouping.[2,4–6] At least one of the two abnormal parameters present would have to be abnormal rectal temperature and/or WBC, using age-specific reference intervals. Two additional parameters were also added to the equine SIRS definition: L-lactate and venous blood glucose concentrations (Table 1).[2,16–22]
4. *Defining septic shock*: Septic shock was defined as sepsis demonstrating cardiovascular compromise persisting after volume resuscitation, and one alteration in physical characteristics, laboratory data or organ function.[3,12–14]

The meeting in August of 2024 served several specific purposes. The manuscript assessing newborn foals from the 2018 meeting was used as a basis for discussion.[1] Based on consensus definitions of sepsis in the human literature (e.g., Sepsis-3),[3] the 2024 meeting participants arrived at the following altered definition of sepsis, with two components:

A. A life-threatening condition involving proven or suspected infection;
B. systemic manifestations of infection.

Proven infection was defined as infection based on positive blood culture *or* positive culture from two different sites. Suspected infection criteria included neutropenia and left shift, using age-specific ranges.[7–14,23–26] Further discussion regarding suspected infection yielded the suggestion of developing a scoring system by the participants, which would be tested over the next 3 years, different from reported sepsis scores of the past.[7–11] Another action point discussed was to develop a scoring system that would help identify part B of the sepsis definition, namely the systemic manifestations of infection. Thus, two scoring systems are to be developed, one for use in the field that would aid practitioners in the early identification of septic or suspected infection/sepsis in newborn and neonatal foals, and a second scoring system for use in hospitals that would help identify systemic manifestations of infection (e.g., organ dysfunction).

The overarching purpose of these 'scoring systems' is threefold:

1. Clinical—recognise septic patients in hospital or in field situations and facilitate identification of systemic manifestations of infection via organ dysfunction.
2. Outcome—predict mortality.
3. Classification for research purposes: comparing apples to apples.

Using data from the 2018 meeting, and the findings and group discussion that occurred at the 2024 meeting, a group was established to develop a simple and quick scoring system (e.g., similar to the quick Sequential Organ Failure Assessment [qSOFA] used in people) for use in the field.[3,27–30] This scoring system would incorporate easily measured physical examination and point-of-care (POC) measurements (Table 2) for early identification of suspected infection/sepsis. The goal of the first scoring system is to provide equine practitioners a practical tool to identify foals with suspected infection and institute early field treatment and/or facilitate referral for hospital treatment. The proposed scoring system would ideally replace the old 'sepsis scores', which are highly variable depending on region/country/hospital.[7–11]

A second working group was tasked with developing an in-hospital assessment, akin to the Sequential Organ Failure Assessment (SOFA) score used in people.[3,27,31] This scoring system is intended to determine organ involvement and the systemic manifestations of infection (not mortality), as stated in Part B of the proposed sepsis definition. Potential criteria that could be used in an equine SOFA scoring system could include alterations in haematologic (leukopenia, neutropenia, toxic neutrophils, N:L ratio, others), renal (creatinine; BUN), nervous (mentation score), respiratory (SpO2, PaO2, Resp rate), hepatic (GGT), coagulation (petechia, platelet count) and/or cardiovascular (HR, extremity temperature,

TABLE 1 Age-based SIRS criteria normal values.

Parameter	Newborn foal (birth to 3 days of age)	Neonatal foal (4–14 days of age)	Juvenile foal (15 days to 6 months of age)	Weanling foal (7 months to 1 year of age)
Rectal temperature	99–102.5°F	99–102.0°F	99–102.0°F	99–101.5°F
Heart rate (bpm)*	60–115	60–120	60–96	40–60
Respiratory rate (bpm)*	30–56	30–56	30–44	20–30
White blood count ($\times 10^3$), 0% band neutrophils	7.0–14.4	4.0–12.5	4.0–12.5	4.0–12.5
Venous L-lactate (mmol/L)	1.0–5.0	1.0–2.5	1.0–2.0	1.0–2.0
Venous blood glucose (mg/dL)	50–160	75–160	75–140	75–110

*Values must be obtained at rest. Criteria were originally presented at the International Veterinary Emergency and Critical Care Symposium, 2020.

TABLE 2 List of potential clinical and clinical pathology characteristics under consideration for scoring systems.

Field scoring	Hospital scoring
Variables to consider	
Altered mentation	Proven or suspected infection/ bacteraemia + systemic manifestations
Extremity temperature	CBC (leukopenia, N:L ratio, N:band ratio, other)
Peripheral pulse	L-lactate
CRT	Organ function (Foal SOFA Score)
MM colour (hyperaemic)	Cardiovascular
Nursing activity (Normal, Decr, Absent)	Renal function (UA, SG, BUN, creatinine)
SIRS criteria: Temp, HR, RR	Central nervous system
POC L-lactate	Others (data driven)
POC glucose	

peripheral pulse, L-lactate) systems. This working group's goal is to develop, establish and test this scoring system in foals.

The 2024 meeting participants altered the definition of septic shock to 'Equine Neonatal Septic Shock', a subset of patients with particularly profound circulatory, cellular and metabolic abnormalities associated with a greater risk of mortality than with sepsis alone. These patients have a vasopressor requirement to maintain mean arterial pressure (MAP) ≥65 mmHg and serum L-lactate >2 mmol/L in the absence of hypovolaemia.[3,12–14]

The various biomarkers potentially associated with sepsis were discussed. Several aspects of the leukogram were considered important: toxic neutrophils, neutrophil:lymphocyte (N:L) ratio, neutropenia and the presence of band neutrophils. Reflecting on these, it becomes obvious that cytologic examination of the blood sample is paramount, particularly observation of toxicity, based on findings from the 2018 data and other published research.[1] The red cell distribution width to platelet ratio (RDW:Plt or RPR) was discussed as a potentially useful biomarker. The RPR is a novel inflammatory indicator that integrates the risk predictions of RDW and platelet count, two independent measures of inflammation, which are associated with adverse outcomes.[26,32,33] This biomarker may prove to be of clinical use. Discussion of serum amyloid A (SAA) concluded that it is not helpful in initial diagnosis and management choices, but may have utility if trends over time are followed.[34] Measurement of L-lactate at initial examination, and repeated frequently during the early treatment period, continues to be a strong indicator of response to treatment of septic foals and the single most useful prognostic indicator of outcome.[35,36] Other areas of interest ranged from Critical Illness-Related Corticosteroid Insufficiency (CIRCI) to measuring IgG to the best practice method of obtaining blood cultures, and pain management in the foal.

Three topics chosen for future investigation were:

1. Develop scoring system(s) for identification of sepsis (requiring less information than the modified sepsis score) similar to the qSOFA or national early warning system (NEWS) in people.
2. Multicentre prospective evaluation of the kinetics of plasma transfusions/antibody persistence in septic foals.
3. Continued assessment of antioxidants in attenuation of clinical signs and/or improvement in outcome in septic newborn/neonatal foals.

In conclusion, the 2024 Working Group made the following recommendations regarding the newborn foal:

1. The proposed definition of foal sepsis is a life-threatening condition involving proven or suspected infection accompanied by systemic manifestations of infection.
2. SIRS should no longer be used in the definition of sepsis in the newborn foal (birth to 3 days of age).
3. The category of 'sick non-septic (SNS)' should not be used as a group classification in studies of foals, and the term 'hospitalised foals' should be used in its place.
4. L-lactate should be measured in sick/abnormal foals and measured repeatedly.
5. The ability to cytologically examine a blood slide is important to diagnosis and case management.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

P. A. Wilkins: Conceptualization; funding acquisition; writing – original draft; writing – review and editing; supervision; project administration; resources. **D. M. Wong:** Conceptualization; writing – review and editing; project administration; supervision; resources; funding acquisition. **DRH Working Group on Foal Sepsis:** Writing – review and editing; resources; conceptualization; funding acquisition.

DATA INTEGRITY STATEMENT

No new data were created or analysed in this study.

ETHICAL ANIMAL RESEARCH

Not applicable.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created.

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