Contents lists available at NCBI

The American Journal of Science and Medical Research

Journal homepage: https://ajsmrjournal.com/

Review Article

Harnessing IgA for the Prevention and Treatment of Respiratory Infections: From Mucosal Immunity to Therapeutic Antibodies

Fawzyah Obeedallah Albaldi

Department of Biology, Faculty of Science, Al-Baha University, 65779-7738 Alaqiq, Albaha, Saudi Arabia.

**Corresponding author:*
E-mail: falbeladi@bu.edu.sa

https://dx.doi.org/10.5281/zenodo.21863433

Received: 21 June 2026
Accepted: 29 July 2026
Published: 09 August 2026

ISSN: 2377-6196
Published by AIRA

Keywords: *Secretory IgA (sIgA), Bovine IgA, Mucosal immunity, Respiratory pathogens, Respiratory tract infections (RTIs), Bovine milk immunoglobulins, Passive immunotherapy.*

ABSTRACT

Mass gatherings, such as the annual Hajj pilgrimage, create complex epidemiological landscapes that facilitate the transmission of respiratory pathogens, including emerging zoonotic threats like MERS-CoV and H5N1. Despite the high incidence of acute respiratory tract infections (ARTIs), current therapeutic strategies primarily systemic vaccines and antivirals often fail to establish robust mucosal protection at the primary portal of entry. This study investigates the potential of secretory IgA (sIgA), specifically bovine-derived sIgA, as a scalable, non-inflammatory mucosal therapeutic to bridge the gap in respiratory infection prevention and treatment. We highlight the unique dual-action mechanism of sIgA, involving both Fab-dependent neutralization and glycan-mediated innate interactions. Recent 2025 data confirming MERS-CoV clusters in Riyadh and the expanded host range of HPAI H5N1 in dairy cattle underscore the urgent need for site-specific countermeasures. We hypothesize that locally sourced bovine sIgA from Saudi Arabian dairy herds possesses distinct functional properties optimized for regional pathogens. Utilizing nebulized, locally derived bovine sIgA represents a paradigm shift in biosecurity and public health, aligning with Saudi Vision 2030 by offering a safe, affordable, and sustainable strategy for protecting vulnerable populations during mass gatherings.

1. Introduction

1.1. Mass Gatherings and the Global Respiratory Burden

Mass gatherings represent one of the most complex and high-stakes arenas in public health. The annual Hajj pilgrimage in the Kingdom of Saudi Arabia (KSA) is the largest recurring human gathering globally, attracting over two million pilgrims from more than 184 nations [1]. This unparalleled convergence of humanity creates a unique epidemiological environment characterized by extreme population density, shared accommodations, and the physical stress of ritual performance. These factors combine to create a "melting pot" for infectious diseases, where pathogens from every corner of the globe can be exchanged, amplified, and ultimately disseminated worldwide upon the pilgrims' return.

Respiratory tract infections (RTIs) are the most pervasive health issue during the Hajj, with clinical surveys consistently reporting incidence rates between 20% and 80% among participants [2]. These infections are not merely a nuisance; they are a major cause of hospitalization and mortality among pilgrims, particularly those who are elderly or have underlying comorbidities [3]. While common viruses like rhinovirus and seasonal influenza are frequent causes of illness, the threat of emerging zoonotic viruses such as MERS-CoV and the potential pandemic risk posed by highly pathogenic avian influenza (HPAI) H5N1 necessitate a state-of-the-art response [4].

Furthermore, the rise of antimicrobial resistance (AMR) has complicated the management of bacterial RTIs. Studies have documented a high prevalence of multi-drug-resistant (MDR) Pseudomonas aeruginosa, Klebsiella pneumoniae, and methicillin-resistant Staphylococcus aureus (MRSA) among Hajj pilgrims [5]. Traditional antibiotic treatments are increasingly failing, and the use of broad-spectrum agents during the pilgrimage may further select for resistant strains, disrupting the host's protective microbiome and leading to secondary infections [6].

Current preventive measures, primarily systemic vaccinations, have saved countless lives but have inherent limitations in the context of mass gatherings. Systemic immunization induces a robust IgG response that prevents severe lower respiratory disease but often fails to provide "sterilizing" mucosal immunity in the upper respiratory tract. This allows for colonization and the spread of pathogens even among the vaccinated. Moreover, the rapid onset of exposure during the

pilgrimage often occurs before a vaccine-induced response can fully mature (which typically takes 10-14 days).

In this context, there is an urgent need for "immediate-acting" mucosal interventions. Secretory IgA (sIgA), the natural gatekeeper of the respiratory and gastrointestinal tracts, provides a biological template for such a solution. By harnessing bovine-derived sIgA, leveraging the Kingdom's industrial dairy capacity, we can develop a scalable, non-inflammatory mucosal shield that can be administered via nebulization to provide instant, broad-spectrum protection. This approach aligns perfectly with the strategic goals of Saudi Vision 2030, fostering biotherapeutic self-sufficiency and national health security.

2. The Evolving Epidemiological Landscape (2025-2026)

2.1. MERS-CoV: Persistent Zoonotic Risk and 2025 Clusters

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) remains a critical threat to regional and global health security. Since its identification in 2012, the virus has caused 2,635 laboratory-confirmed cases and 964 deaths globally, with a staggering case fatality ratio (CFR) of ~37–39% [31], [76]. The Kingdom of Saudi Arabia (KSA) has reported the vast majority of these cases (2,224 cases and 868 deaths) [31].

The year 2025 has seen a continuation of sporadic cases and localized clusters. Between June and December 2025, 17 cases were reported across five regions of the KSA, including Riyadh, Taif, Najran, and Hail [7]. A significant hospital-related cluster of seven cases was identified in Riyadh in 2025, highlighting the persistent risk of nosocomial transmission in healthcare settings [8]. Furthermore, France reported two travel-associated cases in December 2025, involving individuals who had likely been exposed during travel to the Arabian Peninsula [9]. Genomic sequencing conducted by the French health authorities confirmed that these isolates belonged to the same lineage circulating in the Arabian Peninsula, emphasizing the risk of international exportation [10].

Transmission is primarily zoonotic, with dromedary camels serving as the well-established reservoir and host [11]. Human-to-human transmission, while not sustained in the community, remains a major risk in healthcare facilities where delays in diagnosis can lead to significant outbreaks [12]. Symptoms range from asymptomatic or mild respiratory distress to severe pneumonia and multi-organ failure, particularly in individuals with comorbidities such as diabetes, renal failure, and chronic lung disease [13]. The absence of an approved vaccine or specific antiviral therapy for MERS-CoV underscores the criticality of developing mucosal prophylactic shields [14].

2.2. H5N1: Mammalian Adaptation and the Dairy Cattle Interface

The epidemiology of highly pathogenic avian influenza (HPAI) A(H5N1) has entered a worrying new phase. Since 2024, the virus has demonstrated an unprecedented expansion of its host range, infecting numerous mammalian species globally, including foxes, bears, cats, and seals [15]. Most significantly, a widespread outbreak in domestic dairy cattle in the United States has alerted the global health community to the potential for the virus to adapt to large mammalian populations [16].
As of mid-2025, H5N1 has been detected in dairy herds across several US states, with high viral loads found in raw milk [17]. Human cases have been identified among farm workers, presenting with symptoms ranging from mild conjunctivitis to more severe respiratory illness [18]. Genomic sequencing of these viruses has revealed molecular markers associated with mammalian adaptation, such as the PB2 M631L substitution, which enhances the virus's ability to replicate in human cells, and sporadically the PB2 E627K substitution [19].

The global panzootic spread of H5N1 in wild birds means that no region is immune. In the Middle East, the risk of introduction into the intensive dairy and poultry sectors is a major concern [20]. The potential for H5N1 to reassort with human seasonal influenza viruses in a mammalian host remains the primary driver of pandemic risk [21]. This situation necessitates a "One Health" approach, where agricultural biosecurity and human public health are integrated. Utilizing bovine-derived antibodies to protect human health is a perfect example of this synergy, bridging the gap between animal reservoirs and human vulnerability.

2.3. MDR Bacterial Colonization in Mass Gatherings: The "Silent Pandemic"

In addition to viral threats, the "silent pandemic" of antimicrobial resistance (AMR) is a major contributor to Hajj-associated morbidity. The extreme crowding of the pilgrimage facilitates the exchange of MDR bacteria [22]. Studies have documented the rapid acquisition of carbapenem-resistant Enterobacteriaceae and multi-drug-resistant Pseudomonas among pilgrims within days of arrival in the Kingdom [23]. These bacteria can cause severe secondary pneumonia following a viral infection or can lead to difficult-to-treat primary infections in vulnerable individuals. The depletion of the host's natural IgA levels due to stress, overcrowding, and antibiotic use further increases susceptibility to these pathogens [24].

3. Mucosal Immunity: The Body's Sentinel and Primary Defence

3.1. Structural Versatility: The J-Chain and Secretory Component

Secretory IgA (sIgA) is the predominant antibody class at mucosal surfaces, where it serves as the first line of defense. Its unique structure is the result of a complex biosynthetic pathway designed for maximum stability and function in hostile environments like the respiratory and gastrointestinal tracts.

sIgA is primarily dimeric or polymeric, consisting of two or more IgA monomers linked by a 15-kDa joining (J) chain [25]. This dimeric complex is produced by plasma cells in the lamina propria and is then transported across epithelial cells by the polymeric immunoglobulin receptor (pIgR). During this process (transcytosis), the pIgR is cleaved, and a portion of the 70-kDa secretory component (SC) remains covalently or non-covalently attached to the antibody complex [26].

The SC provides two essential functions:

Proteolytic Resistance: The SC physically wraps around the IgA monomers, masking sensitive sites in the hinge region that are the primary targets for bacterial proteases (e.g., S. pneumoniae IgA1 protease). This structural protection allows sIgA to remain functional for extended periods within the proteolytic enzymatic landscape of the respiratory mucus [27].

Mucus Retention and Adhesion: The glycans on the SC interact with mucin proteins and other components of the mucosal matrix, ensuring that the antibody remains concentrated at the epithelial interface rather than being rapidly cleared [28].

3.2. Mechanisms of Action: Fab-Dependent Adaptive Neutralization

The protective efficacy of sIgA is multifaceted, combining adaptive and innate immune principles. The Fab-dependent mechanism is the classical antibody-mediated defense. The variable regions (Fab) of the IgA molecules bind with high avidity to specific microbial proteins, such as the Spike protein of MERS-CoV or the Hemagglutinin of influenza viruses.

Because sIgA is multivalent (containing four or more binding sites), it is exceptionally effective at agglutinating pathogens—clumping them together to prevent their attachment to host cell receptors—a process known as "immune exclusion" [29]. Agglutinated pathogens are then trapped in the mucus layer and cleared via the mucociliary escalator or gastrointestinal peristalsis. This prevents the initial colonization and infection of the underlying epithelial cells.

3.3. Mechanisms of Action: Glycan-Mediated Decoy Immunity

A highly significant but often overlooked mechanism involves the glycans attached to the secretory component and the IgA heavy chains. These glycans act as "decoy receptors" that provide a broad-spectrum, innate layer of protection [70]. Many respiratory and gastrointestinal pathogens, including influenza viruses, Streptococcus pneumoniae, and Helicobacter pylori, use their own lectin-like proteins to bind to specific sugars on the human host epithelium [30].

sIgA carries a diverse array of these same sugar motifs (e.g., sialic acid, fucose, and galactose). These glycans intercept the pathogens, effectively "tricking" them into binding to the antibody rather than the host cell [31]. For instance, sialic acids on sIgA can bind to the hemagglutinin of influenza viruses, while other glycan motifs can block the CbpA protein of S. pneumoniae [32]. This mechanism is non-specific and provides broad-spectrum protection against a wide range of bacteria and viruses, even those for which the host has not developed specific adaptive immunity.

4. Bovine sIgA: A Scalable and Sustainable Biotherapeutic Platform

4.1. Comparative Analysis: Human vs. Bovine sIgA

While human sIgA is the "gold standard" for mucosal immunity, its production at the scale required for global mass gatherings is technically and economically unfeasible. Bovine-derived sIgA offers a viable and superior alternative for large-scale pharmaceutical applications. Bovine colostrum and milk are naturally enriched with sIgA and IgG, and the infrastructure of the global dairy industry is already optimized for the processing of these biological products.

Bovine sIgA is structurally similar to human sIgA, containing both the J-chain and the secretory component, and it is equally, if not more, resistant to proteolysis in the human gut and respiratory tract [33]. Furthermore, bovine antibodies are already in successful clinical use; products like EnteraGam® (serum-derived bovine immunoglobulin, SBI) have a long-standing safety record in humans, proving that bovine-derived immunoglobulins are well-tolerated and functional when administered to patients [34, 42-44].

Table-1. Comparative Analysis of Human and Bovine sIgA

Feature	Human sIgA	Bovine sIgA
Primary Structure	Dimeric / Polymeric	Polymeric (Dimer/Trimer/Tetramer)
Source	Human Plasma / Colostrum	Bovine Colostrum / Milk
Scalability	Low (Donor-limited; Expensive)	High (Industrial scale; Sustainable)
Protease Resistance	High (SC-protected)	Very High (SC-protected)
Glycan Profiling	Complex human-type glycans	Distinct bovine glyco-motifs
Cost of Production	Extremely High	Moderate to Low
Clinical Safety	High	Proven (e.g., EnteraGam, SBI)
Availability	Rare / Boutique	Readily Available / Scalable

4.2. The Hypothesis of Geographic Variability (Saudi Arabia vs. Global)

An innovative aspect of this research is the hypothesis that bovine sIgA varies geographically. The immune repertoire and glycosylation patterns of a cow are a direct reflection of its environment and the pathogens it encounters throughout its life. We hypothesize that bovine sIgA from Saudi Arabian dairy herds possesses distinct structural and functional characteristics that make it uniquely suited to protect pilgrims during the Hajj. Saudi Arabian sIgA is likely enriched with antibodies and glycan decoys that are specifically "tuned" to the pathogens endemic to the Arabian Peninsula, such as local MERS-CoV-like coronaviruses and regional MDR bacterial strains (e.g., VIM-producing P. aeruginosa found in Makkah [5]). The extreme heat and arid climate of the Kingdom may also influence the glycosylation machinery of the bovine mammary gland, leading to distinct glycan decoy profiles compared to temperate regions.

By characterizing the glycan profiles and binding specificities of sIgA from this region, we can select the most effective components to create a comprehensive mucosal shield. A "locally sourced" Saudi Arabian biotherapeutic would be biologically optimized for the specific "melting pot" of pathogens encountered during the pilgrimage.

5. Evidence Matrix and Comparative Pathogen Analysis

The following tables summarize the current evidence supporting the use of bovine-derived immunoglobulins and the epidemiological context that necessitates their deployment in the Middle East.

Table-2. Evidence Matrix of sIgA/Bovine Antibody Efficacy

Study / Source	Target Pathogen(s)	Evidence / Findings
EnteraGam® (SBI)	GI Pathogens / Toxins	FDA-regulated medical food; reduces inflammation and neutralizes toxins**[35]**.
Maruthachalam et al.	*S. pneumoniae*	Secretory component glycans block pIgR-mediated bacterial invasion**[36]**.
de Fays et al.	H5N1 Influenza	Mucosal antibody response is a critical marker for human protection**[37]**.
Alkhattabi et al.	Regional RTIs	High burden of child RTIs in KSA highlights the need for new preventatives**[38]**.

Table-3. Comparative Epidemiology of High-Risk Respiratory Pathogens (2025 Context)

Pathogen	Primary Reservoir	2025 Status / Risk	Public Health Impact
MERS-CoV	Dromedary Camels	19 cases (2025); 17 in KSA; Riyadh hospital clusters. **[39]**	**High** (CFR ~37%); Risk of Hajj dissemination.
H5N1 (Avian Flu)	Wild Birds / Cattle	Global panzootic; Mammalian adaptation in US cattle**[40]**	**Moderate** (Pandemic potential); One Health concern.
MDR Bacteria	Hospital / Humans	Rapid acquisition during Hajj; carbapenem resistance **[41]**.	**Critical** (Antibiotic failure); Major Hajj morbidity.

6. Biomanufacturing, Formulation, and Nebulization Dynamics

The production of therapeutic bovine sIgA involves several critical technological steps to ensure a high-purity, stable, and effective product:

Hyperimmunization: Cows are immunized with specific antigens (e.g., MERS-CoV Spike protein, H5N1 hemagglutinin) to "boost" the concentration of specific adaptive antibodies in their colostrum and milk. This creates a "hyperimmune" product with targeted neutralizing power.

Fractionation and Purification: Advanced membrane filtration (ultrafiltration/diafiltration) and chromatography are used to isolate the sIgA fraction while removing allergens (like beta-lactoglobulin) and non-essential proteins. The preservation of the secretory component and the polymeric state is essential for functional efficacy.

Formulation and Stability: The purified sIgA is formulated into a stable liquid or lyophilized powder. Maintaining stability in the extreme heat of the Saudi Arabian summer is a key requirement, making sIgA's natural robustness a major advantage.

Nebulization Dynamics: Delivering large, polymeric proteins like sIgA via nebulization requires specialized vibrating mesh or ultrasonic nebulizers. These devices must be optimized to generate a particle size (1-5 microns) that ensures deep lung and nasopharyngeal deposition while maintaining the structural integrity of the antibody.

7. Limitations and Research Gaps: Toward Clinical Translation

IgA based biologics represent an emerging approach for enhancing mucosal immunity, yet several limitations must be addressed before they can be translated into practical applications. A major challenge lies in defining the optimal dosing, delivery method, and duration of effect needed to maintain consistent mucosal protection, as these parameters remain insufficiently characterized. In addition, although oral IgA preparations have demonstrated a strong safety record, the long term tolerability of inhaled or nebulized IgA within the respiratory tract requires thorough clinical evaluation to exclude potential immunogenic or inflammatory effects. Regulatory considerations also present obstacles, as IgA derived from non human sources occupies a complex space that demands clear standards for manufacturing, quality control, and approval pathways. Finally, the breadth of IgA activity is inherently shaped by its antigen exposure history, raising concerns about cross reactivity and the ability to provide broad protection against diverse microbial strains encountered in real world environments. Together, these limitations underscore the need for further mechanistic studies and controlled clinical trials to fully define the feasibility and safety of IgA based mucosal interventions.

8. Conclusion

The field of mucosal immunology is entering a transformative era. The convergence of persistent and emerging respiratory threats underscores the urgent need for innovative, scalable, and biologically grounded interventions. Secretory IgA, with its combined adaptive and innate protective functions and exceptional structural stability, offers a compelling blueprint for a universal mucosal defense capable of addressing diverse pathogens. Leveraging large scale bovine IgA production provides a practical pathway toward developing next generation nebulized biotherapeutics designed to reinforce the respiratory mucosa. Such an approach aligns with global efforts to enhance self sufficiency in biologics, strengthen public health resilience, and expand accessible tools for respiratory pathogen mitigation. Ultimately, the natural sentinel of our mucosal surfaces—secretory IgA—may represent one of the most effective foundations for future strategies aimed at reducing the burden of airborne infectious diseases.

Competing interests:

The authors declare that they have no competing interests

References

[1] Petrzelova, D., L. Raskova Kafkova, J. Skarda, Z. Perutka, M. Krupka, M. Sebela, Z. Jiraskova Zakostelska, Z. Reiss, K. Stepanova, and D. Srutkova, Polymeric IgA with unique glycans protects against necrotoxigenic E. coli O55 infection in an animal model. The Journal of Immunology, 2026. 215(2): p. vkaf300.

[2] Fakhoury, A. and A. Fakih, Government intervention and business response as determinants of business

continuity amid COVID-19: the case of Jordan and Morocco. International Journal of Economic Policy in Emerging Economies, 2023. 17(2): p. 196-219.
[3] Organization, W.H., Middle East respiratory syndrome coronavirus-Kingdom of Saudi Arabia. 2025. 2025.
[4] Alharbi, N.M.J., N.F. Tashkandi, A.M. Banjar, A.Y. Alotaibi, S. Al-Harbi, A.M.A. Alqarni, Y.A. Alharbi, H.H. Alkenani, A.A. Bokhari, and A. Banjar, Pattern of antibiotic use among children with acute respiratory infections in Saudi Arabia: Clinical assessment. Cureus, 2024. 16(2).
[5] Al-Zahrani, I.A. and B.M. Al-Ahmadi, Dissemination of VIM-producing Pseudomonas aeruginosa associated with high-risk clone ST654 in a tertiary and quaternary hospital in Makkah, Saudi Arabia. Journal of Chemotherapy, 2021. 33(1): p. 12-20.
[6] Bokhary, H., H. Research Team, O. Barasheed, H.B. Othman, B. Saha, H. Rashid, G.A. Hill-Cawthorne, and M. Abd El Ghany, Evaluation of the rate, pattern and appropriateness of antibiotic prescription in a cohort of pilgrims suffering from upper respiratory tract infection during the 2018 Hajj season. Access Microbiology, 2022. 4(4): p. 000338.
[7] O'Connor, P. and G. Assaker, COVID-19's effects on future pro-environmental traveler behavior: an empirical examination using norm activation, economic sacrifices, and risk perception theories. Journal of Sustainable Tourism, 2021. 30(1): p. 89-107.
[8] Abdelazim, M., R. Abdelkader, A. Ali, M.A. Shahein, Z. Tadesse, A. Saad, A. Mansour, S.F. Ali, M. Atea, and E. Gardner, A longitudinal study of Middle East respiratory syndrome coronavirus (MERS-CoV) in dromedary camels. BMC veterinary research, 2023. 19(1): p. 228.
[9] McLean, G.R., Vaccine strategies to induce broadly protective immunity to rhinoviruses. Human vaccines & immunotherapeutics, 2020. 16(3): p. 684-686.
[10] Widjaja, I., C. Wang, R. van Haperen, J. Gutiérrez-Álvarez, B. van Dieren, N.M. Okba, V.S. Raj, W. Li, R. Fernandez-Delgado, and F. Grosveld, Towards a solution to MERS: protective human monoclonal antibodies targeting different domains and functions of the MERS-coronavirus spike glycoprotein. Emerging microbes & infections, 2019. 8(1): p. 516-530.
[11] Almaghlouth, I., T. Islam, N. Alamro, A. Alsultan, A. Alfadda, S. Al-Muhsen, A. Almasry, M.A. Almadi, A. Hersi, and A. BaHammam, Mapping COVID-19 related research from Saudi Arabia, a scoping review: between reality and dreams. Saudi medical journal, 2020. 41(8): p. 791.
[12] Alreeme, S., H. Bokhary, and A.T. Craig, Transmission of antimicrobial resistant bacteria at the Hajj: a scoping review. International Journal of Environmental Research and Public Health, 2022. 19(21): p. 14134.
[13] Guerrero-Bustamante, C.A. and G.F. Hatfull, Bacteriophage tRNA-dependent lysogeny: requirement of phage-encoded tRNA genes for establishment of lysogeny. MBio, 2024. 15(2): p. e03260-23.
[14] Breugem, T.I., S. Riesebosch, J. Zhang, A.Z. Mykytyn, L. Krabbendam, N. Groen, S. Baptista Varela, D. Schipper, P.B. van den Doel, and R. van Acker, Variable DPP4 expression in multiciliated cells of the human nasal epithelium as a determinant for MERS-CoV tropism. Proceedings of the National Academy of Sciences, 2025. 122(11): p. e2410630122.
[15] Moț, D., E. Tîrziu, and L. Olariu-Jurca, The Evolution of Highly Pathogenic Avian Influenza in Recent Years in the New Geographical Regions of the World and in New Species. SCIENTIFIC PAPERS ANIMAL SCIENCE AND BIOTECHNOLOGIES, 2026. 59(1): p. 449-460.
[16] Haman, K.H., S.F. Pearson, J. Brown, L.A. Frisbie, S. Penhallegon, A.M. Falghoush, R.M. Wolking, B.K. Torrevillas, K.R. Taylor, and K.R. Snekvik, A comprehensive epidemiological approach documenting an outbreak of H5N1 highly pathogenic avian influenza virus clade 2.3. 4.4 b among gulls, terns, and harbor seals in the Northeastern Pacific. Frontiers in Veterinary Science, 2024. 11: p. 1483922.
[17] Roland-Holst, D. and K. Ning, Transboundary Livestock Disease Control: Insights from the PRC and other Greater Mekong Subregion Countries. 2025.
[18] Windsor, P.A., Perspectives on progression of transboundary disease, one health and ecosystem health management in the Greater Mekong Subregion and beyond. Animal Production Science, 2024. 64(11): p. AN23431.
[19] Gongal, G., H. Rahman, K.C. Thakuri, and K. Vijayalakshmy, An overview of transboundary animal diseases of viral origin in South Asia: what needs to be done? Veterinary sciences, 2022. 9(11): p. 586.
[20] Kamel, M., S. Aleya, W.T. Almagharbeh, L. Aleya, and M.M. Abdel-Daim, The emergence of highly pathogenic avian influenza H5N1 in dairy cattle: implications for public health, animal health, and pandemic preparedness. European Journal of Clinical Microbiology & Infectious Diseases, 2025. 44(8): p. 1817-1833.
[21] El-Bidawy, M.H., I. Mohammad, M.R. Ansari, M.I. Hajelbashir, M.S. Khan, M.M. Poyil, M.N. Bari, A.M. Arafah, M.A. Kamal, and S.T.M. Ahsan, Highly Pathogenic Avian Influenza: Tracking the Progression from IAV (H5N1) to IAV (H7N9) and Preparing for Emerging Challenges. Microorganisms, 2025. 14(1): p. 12.
[22] Doumith, M., S. Alhassinah, A. Alswaji, M. Alzayer, E. Alrashidi, L. Okdah, S. Aljohani, N.A.S. Group, H.H. Balkhy, and M.F. Alghoribi, Genomic characterization of carbapenem-non-susceptible Pseudomonas aeruginosa clinical isolates from Saudi Arabia revealed a global dissemination of GES-5-producing ST235 and VIM-2-producing ST233 sub-lineages. Frontiers in microbiology, 2022. 12: p. 765113.
[23] Kolivand, P., P. Saberian, P. Namdar, S. Rajaie, F. Karimi, T. Doroudi, A. Marashi, M. Behzadifar, A. Parvari, and S.J. Ehsanzadeh, Pattern of Antibiotic Use and Economic Impact among Hospitalized Iranian Hajj Pilgrims. Trauma, 2024. 120(13.2): p. 13.2.
[24] Choi, D., S.J. Jang, S. Choi, S. Park, W.-K. Kim, G. Lee, C. Lee, and G. Ko, Oral administration of Limosilactobacillus reuteri KBL346 ameliorates influenza virus A/PR8 infection in mouse. Probiotics and Antimicrobial Proteins, 2025. 17(5): p. 3546-3558.
[25] Cui, C., X. Feng, Q. Min, C. Lu, Z. Wen, X. Meng, R. Zhang, L. Dong, and J.-Y. Wang, Cooperative control of IgA synthesis and secretion by MZB1 and the J chain. Frontiers in Immunology, 2026. 17: p. 1744147.
[26] Frey, A., L.P. Lunding, and M. Wegmann, The dual role of the airway epithelium in asthma: active barrier and regulator of inflammation. Cells, 2023. 12(18): p. 2208.
[27] Sun, M., J. Ju, H. Xu, and Y. Wang, Intestinal fungi and antifungal secretory immunoglobulin A in Crohn's disease. Frontiers in Immunology, 2023. 14: p. 1177504.

[28] Wu, C.M., K.M. Wheeler, G. Cárcamo-Oyarce, K. Aoki, A. McShane, S.S. Datta, J.L. Mark Welch, M. Tiemeyer, A.L. Griffen, and K. Ribbeck, Mucin glycans drive oral microbial community composition and function. npj Biofilms and Microbiomes, 2023. 9(1): p. 11.

[29] Ohtani, M., H. Fujii, T. Watanabe, O. Ohara, M. Maruya, S. Fagarasan, T. Hoshii, A. Hirao, S. Koyasu, and M. Kubo, mTORC1-independent IgA production: a unique pathway for gut immune homeostasis. International immunology, 2026. 38(3): p. 185-196.

[30] Vilhena, C., S. Du, M. Battista, M. Westermann, T. Kohler, S. Hammerschmidt, and P.F. Zipfel, The choline-binding proteins PspA, PspC, and LytA of Streptococcus pneumoniae and their interaction with human endothelial and red blood cells. Infection and immunity, 2023. 91(9): p. e00154-23.

[31] Mauser, H.D., T.E. Keyzer, J.M. Surma, N.G. Alexander, W.D. Cutts, S.F. Hathcock, K.H. Lackey, D.W. Lam, J.A. Thornton, and N. Vollmuth, Stem cell-derived brain-like endothelial cells to interrogate Streptococcus pneumoniae interaction with brain endothelium. Virulence, 2025. 16(1): p. 2564281.

[32] Mebus, V.H., S. De, L.M. Busch, M. Gesell Salazar, R. Schlüter, U. Völker, S. Hammerschmidt, and D. Frees, The ClpXP protease and the ClpX unfoldase control virulence, cell division, and autolysis in Streptococcus pneumoniae. Microbiology Spectrum, 2025. 13(7): p. e00804-25.

[33] Lawal, O., A.O. Olaniyi, U.C. Tochukwu, C. Rono, M.J. Badmus, M.O. Abdulkareem, U.M. Odinaka, I.O. Orenolu, and U.N. Chidimma, Mucosal Immune Markers and Their Impact on Antimicrobial Resistance: A Systematic Review. Journal of Clinical Medicine of Kazakhstan, 2025. 22(6): p. 109-116.

[34] Eker, F., E. Akdaşçi, H. Duman, Y.M. Yalçıntaş, A.A. Canbolat, A.E. Kalkan, S. Karav, and D. Šamec, Antimicrobial properties of colostrum and milk. Antibiotics, 2024. 13(3): p. 251.

[35] Aaron, D.G., The fall of FDA review. Yale J. Health Pol'y L. & Ethics, 2023. 22: p. 95.

[36] Maruthachalam, B.V., A. Zwolak, X. Lin-Schmidt, E. Keough, N. Tamot, S. Venkataramani, B. Geist, S. Singh, and R. Ganesan. Discovery and characterization of single-domain antibodies for polymeric Ig receptor-mediated mucosal delivery of biologics. in MAbs. 2020. Taylor & Francis.

[37] de Fays, C., F.M. Carlier, S. Gohy, and C. Pilette, Secretory immunoglobulin a immunity in chronic obstructive respiratory diseases. Cells, 2022. 11(8): p. 1324.

[38] Alkhattabi, F., G. Askar, A. Arefi, R. Saber, R. Alhuthil, and A. Alrabiah, Assessment of current child abuse policies in Saudi Arabia within the healthcare context: A comprehensive review. International Journal of Pediatrics and Adolescent Medicine, 2024. 11(1): p. 2-9.

[39] Al-Raddadi, R.M., O.I. Shabouni, Z.M. Alraddadi, A.H. Alzalabani, A.M. Al-Asmari, A. Ibrahim, A. Almarashi, and T.A. Madani, Burden of Middle East respiratory syndrome coronavirus infection in Saudi Arabia. Journal of Infection and Public Health, 2020. 13(5): p. 692-696.

[40] Peacock, T.P., L. Moncla, G. Dudas, D. VanInsberghe, K. Sukhova, J.O. Lloyd-Smith, M. Worobey, A.C. Lowen, and M.I. Nelson, The global H5N1 influenza panzootic in mammals. Nature, 2025. 637(8045): p. 304-313.

[41] Pao, L.T., M. Tashani, C. King, H. Rashid, and A. Khatami, Antimicrobial resistance associated with mass gatherings: a systematic review. Tropical Medicine and Infectious Disease, 2024. 10(1): p. 2.

[42] Swapna, K., Srujana, M., & Mamidala, E. (2024). Identification of steroidal cardenolides from Calotropis procera as novel HIV-1 PR inhibitors: A molecular docking & molecular dynamics simulation study. The Indian journal of medical research, 160(1), 78.

[43] Lunavath, V., & Mamidala, E. (2013). Preliminary phytochemical screening and antibacterial studies of the leaves of Eclipta alba (L). Int J Pharma Biosci, 4, 380-4.

[44] Sucharitha, E., & Estari, M. (2013). Evaluation of antidiabetic activity of medicinal plant extracts used by tribal communities in rural areas of Warangal district, Andhra Pradesh, India. Biology and medicine, 5, 20.