BioTechnologia vol. 107(4) • pp. 1-16 • 2026
Journal of Biotechnology, Computational Biology and Bionanotechnology REVIEW PAPER
https://doi.org/10.5114/bta/226161

CC BY 4.0

Applications of IgY technology in diagnosis and treatment: a review

Letícia Coelho da Cruz[1*], Juliane Corręa Glória[2,3*], Caio Coutinho de Souza[1], Jehovanna Victoria Marín Salgado[4], Jander Matos Guimarães[5], Luis André Morais Mariúba[1,2,3,6,7]

[1]Multi-Institutional Graduate Program in Biotechnology, Federal University of Amazonas (PPGBIOTEC-UFAM), Manaus, AM, Brazil

[2]Oswaldo Cruz Foundation, Leônidas and Maria Deane Institute (ILMD-FIOCRUZ), Manaus, AM, Brazil

[3]INCT-CONEXÃO BIO3TOX – National Institute of Science and Technology for Research and Excellence in Western/Eastern Amazonian Knowledge in Biodiversity, Biotechnology, Biometeorology, and Toxicology Applied to One Health, Fiocruz Rondônia, Porto Velho, RO, Brazil

[4]Undergraduate Program in Biotechnology, Federal University of Amazonas, Manaus, AM, Brazil

[5]Amazonas State University, Multi-User Center for Biomedical Phenomena Analysis, Manaus, AM, Brazil

[6]Graduate Program in Basic and Applied Immunology, Federal University of Amazonas (PPGIBA-UFAM), Manaus, AM, Brazil

[7]Graduate Program in Host–Pathogen Interaction Biology, Oswaldo Cruz Foundation, Leônidas and Maria Deane Institute (ILMD-FIOCRUZ), Manaus, AM, Brazil

**These authors contributed equally to this work.*

Received: 4 March 2026, **Revised:** 11 July 2026, **Accepted:** 20 July 2026

Abstract

Derived from the egg yolk of immunized hens, immunoglobulin Y (IgY) represents a highly versatile alternative to mammalian immunoglobulins for diagnostic and therapeutic applications. Unlike conventional mammalian-based immunoglobulin G antibodies, IgY can be isolated noninvasively from egg yolks, upholding animal welfare standards while facilitating large-scale, cost-effective production. In addition to these ethical and economic advantages, IgY exhibits high antigen specificity, strong affinity, and negligible cross-reactivity with mammalian Fc receptors, rheumatoid factors, and complement components – critical attributes that minimize background interference in immunoassays. These properties render IgY ideal for immunodiagnostic platforms, including enzyme-linked immunosorbent assay, immunochromatographic assays, and biosensor-based detection systems. This review highlights recent advances in IgY technology, with particular emphasis on immunization strategies, extraction and purification protocols, and methods to optimize antibody stability and activity. The paper also discusses the therapeutic potential of IgY, specifically regarding pathogen neutralization, the inhibition of microbial adhesion, the modulation of intestinal microbiota, and topical applications targeting mucosal and skin infections. Collectively, these findings reinforce IgY as a robust and innovative tool for translational research, clinical diagnostics, and alternative immunotherapeutic strategies.

Key words: IgY technology, diagnosis, treatment, antigen detection, polyclonal antibodies

Introduction

The public health emergency caused by the novel coronavirus underscored the critical need for rapid, accurate diagnostics and effective therapeutics capable of meeting immense global demand. In this context, immunoglobulin Y (IgY) technology has emerged as a promising, versatile option for generating biological inputs, gaining considerable attention over recent decades.

Corresponding author: Luis André Morais Mariúba, Instituto Leônidas e Maria Deane (ILMD-FIOCRUZ), Rua Teresina, 476, Adrianópolis, CEP 69057-070, Manaus, AM, Brazil, e-mail: andre.mariuba@fiocruz.br

IgY, a class of immunoglobulin found in birds, reptiles, and lungfish, serves as a functional analog to mammalian immunoglobulin G (IgG). IgY antibodies are transferred from the maternal bloodstream to the developing yolk via specific receptors, where they are stored and provide embryonic protection. The production of these antibodies has been characterized across various animal models (Haese et al. 2015; Najdi et al. 2016; Pacheco et al. 2023). In the 1980s, Klemperer first reported the serum-to-yolk transfer of IgY antibodies in birds (Zhang X et al. 2021). Currently, the number of publications, citations, and research institutions leveraging IgY technology is expanding rapidly, particularly over the past decade. This growth has accelerated technological maturity for commercialization (Wu et al. 2022), driving a market value of approximately 2 billion US dollars annually (Conroy et al. 2017).

Although IgY shares some features with IgG, the phylogenetic distance between birds and mammals offers significant diagnostic and therapeutic advantages for managing medically important diseases. Crucially, IgY minimizes the likelihood of false-positive results and assay interferences (Sivaprasad et al. 2020). Compared with mammalian IgG, IgY provides reduced immunogenicity, higher specificity, fewer adverse effects, and ease of large-scale production and purification (Ge et al. 2024). In addition, IgY exhibits exceptional stability; it can be stored at 4°C for approximately 10 years without significant loss of biological activity, and remains stable at room temperature for 6 months or at 37°C for 1 month (Abbas et al. 2019). These characteristics are highly beneficial for high-throughput industries, reducing the costs associated with cold storage facilities and facilitating diagnostic and immunotherapeutic applications in remote areas due to greater stability.

Despite these advantages, mammalian IgG antibodies remain the most widely used molecules for the detection of human diseases. However, IgG production presents distinct drawbacks, primarily the low concentrations of target-specific antibodies generated by mammalian immunization – often requiring multiple animals to achieve adequate yields – alongside ethical concerns regarding invasive procedures such as repeated bleeding and, in some cases, euthanasia (Michelchen et al. 2020). Conversely, IgY production offers an efficient and ethically favorable alternative by providing a noninvasive and cost-effective approach that substantially reduces animal requirements (Schade and Hlinak 1996).

Given these benefits, the adoption of IgY biomolecules has expanded across veterinary, biomedical, and biotechnological fields as a cornerstone for immunotherapies and immunodiagnostics targeting diverse infectious diseases (Hridya et al. 2025; Thirumalai et al. 2019). Accordingly, this review highlights advances from the past decade in polyclonal IgY-based immunoassays and immunotherapies, detailing different methodological approaches and evaluating their performance.

Obtaining polyclonal IgY antibodies

IgY technology relies on the immunization of birds with a target antigen (proteins, extracts, or peptides) for the synthesis of IgY antibodies, which are subsequently extracted from the egg yolk (Li et al. 2015; Schade et al. 2005; Sudjarwo et al. 2014). Current approaches utilize distinct antibody extraction strategies, including precipitation using solvents, sulfates, polymers, or pH adjustments. Following extraction, IgY is purified using affinity chromatography, size-exclusion chromatography, or gel filtration (Amro et al. 2018; Bizanov 2017; Pauly et al. 2011; Tong et al. 2015).

Bizanov (2017) evaluated IgY purification techniques based on water dilution under acidic conditions or the use of acidic media, solvent combinations, 3.5% polyethylene glycol, or natural gums (polyanionic polysaccharides). The author concluded that water dilution combined with chromatography and filtration provides optimal IgY recovery and is readily scalable for industrial applications (Bizanov 2017).

A single hen can lay approximately 300–eggs annually, yielding roughly 17–35 g of total IgY. However, production cost per gram or milligram is influenced by several factors, such as animal husbandry (housing, feeding), extraction and purification protocols, research and development, and production scale (Tabll et al. 2024). Amro et al. (2018) demonstrated that breed selection critically impacts IgY yields; specifically, Rhode Island Red chickens produced over twofold higher amounts of antibodies compared with Single-Comb White Leghorn chickens. Overall, IgY technology represents a highly versatile biotechnological tool. The process of generating specific antibodies for diagnostic applications is illustrated in Figure 1.

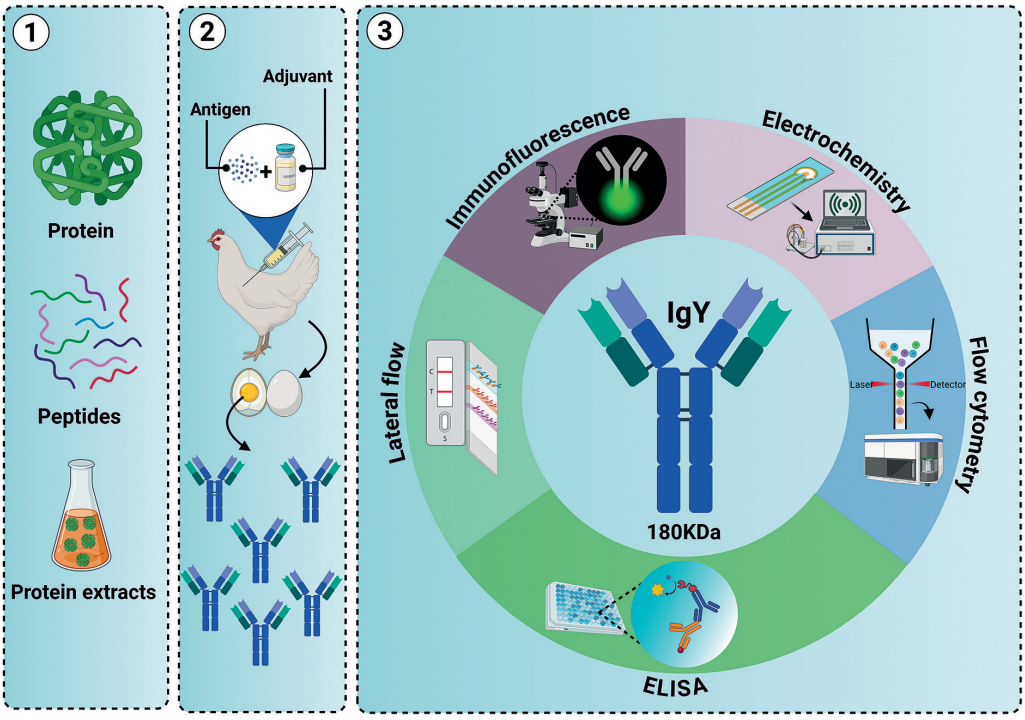

Figure 1. Schematic representation of the immunoglobulin Y (IgY) technology workflow.
ELISA – enzyme-linked immunosorbent assay

Applications of IgY

Over recent decades, studies evaluating the *in vitro* and *in vivo* antibacterial, antiviral, antifungal, and antiparasitic activities of IgY have increased significantly. Due to its unique properties, IgY holds broad prophylactic and therapeutic utility in human and veterinary medicine (Leiva et al. 2020); notable clinical applications include the management of periodontitis, gingivitis, dental caries, enteric infectious diseases, gastric ulcers, calf diarrhea, and bovine mastitis (Wu et al. 2022).

Furthermore, IgY antibodies have the potential to serve as a valuable tool in research, diagnostics, and therapeutics due to their distinct functional properties. These include a broader epitope recognition capacity relative to mammalian-derived IgG, the inability to activate the human complement system, high-scale production yields, and minimized ethical concerns regarding animal experimentation (Tabll et al. 2024).

Consequently, the development of IgY-based immunodiagnostic assays has attracted significant attention, with numerous reviews documenting the efficacy of IgY antibodies in diagnosing both infectious and chronic diseases. To date, IgY antibodies have been successfully incorporated into diverse immunoassay formats, including enzyme-linked immunosorbent assay (ELISA), Western blot, immunohistochemistry, immunochromatography, immunofluorescence, and biosensor systems, for diagnostic purposes in both human and veterinary medicine (Pacheco et al. 2023).

Applications of IgY antibodies in immunoassays

Bacterial infection

As one of the most widely used diagnostic platforms, ELISA requires highly specific antibodies for biomarker detection. IgY antibodies exhibit excellent applicability in ELISA-based tests, enabling the diagnosis of various infectious diseases.

For instance, IgY antibodies were used in the development of a sandwich ELISA targeting the outer membrane protein W (OmpW) and cytotoxin B (CtxB) of *Vibrio cholerae* (Bayat et al. 2018). Given the fluctuations in the number of cases over the years and nonspecific nature of symptoms, rapid and accurate surveillance of cholera is critical (Azman et al. 2020). IgY-based immunoassay achieved a detection limit of 10^3 CFU/ml for the OmpW protein and 33 pg/ml for the recombinant CtxB protein, confirming high sensitivity in antigen recognition (Bayat et al. 2018).

To improve the diagnosis of tuberculosis – one of the deadliest diseases caused by a single infectious agent (World Health Organization 2020a) – Chen et al. (2013) developed an innovative method to immobilize IgY antibodies against the *Mycobacterium tuberculosis* (MBTC) complex onto alginate microspheres. This diagnostic tool achieved diagnostic specificity comparable to ELISA, while the large surface area of the microspheres enhanced the detection limit, which was assessed by measuring the fluorescence intensity of the labeled target bacteria.

Novel pathogen antigen detection methods have emerged rapidly over the past decade. Kota et al. (2020) developed an immunocapture polymerase chain reaction (PCR) assay using IgY antibodies against *Staphylococcus aureus* protein A to detect the bacterium in clinical, environmental, and food samples. Following antibody-mediated bacterial capture and cell lysis, bacterial DNA was subjected to PCR. The assay showed no cross-reactivity with other Gram-positive or Gram-negative foodborne pathogens, reaching a detection limit of $> 10^2$ colony-forming units (CFU)/ml in broth cultures and 10^2–10^3 CFU/ml in natural samples. Separately, a hybrid sandwich aptamer-linked immunosorbent assay was developed for staphylococcal enterotoxin B (SEB), employing anti-SEB IgY as the capture antibody and biotinylated aptamers for detection. This assay exhibited a detection limit of 50 ng/ml, representing a cost-effective approach for monitoring SEB in food and environmental matrices (Mudili et al. 2015).

Furthermore, Lv et al. (2024) immunized chickens with inactivated *Leptospira* to produce antigen-specific IgY antibodies and evaluate extraction yield and therapeutic efficacy. Microagglutination and ELISA indicated that IgY obtained from the eggs of vaccinated birds specifically bound the pathogen, while subsequent *in vivo* testing in hamsters revealed that early IgY administration increased survival rate to 100%.

Similarly, Moosavi et al. (2025) evaluated the *in vitro* inhibitory activity of IgY antibodies elicited by various *Salmonella typhimurium* antigens. Antibody specificity was validated via Western blot, while indirect ELISA quantified IgY binding in both serum and egg yolk. The results indicate that tailored immunization protocols paired with optimal antigen selection establish a solid basis for future vaccine development.

Viral infection

In the context of viral infections, Budama-Kilinc et al. (2018) first produced IgY antibodies targeting the matrix protein 2 extracellular domain (M2e) peptide for influenza A detection. When conjugated to latex particles, these antibodies detected two virus strains. Subsequently, Ozkan et al. (2019) used the same M2e antigen to develop a sandwich ELISA employing alkaline phosphatase-labeled IgY antibodies. The assay demonstrated high concordance with reverse transcription PCR (RT-PCR) results, although additional studies are warranted to comprehensively assess its sensitivity and specificity.

To detect hepatitis A virus – a pathogen typically transmitted via the fecal–oral route and associated with poor sanitary and socioeconomic conditions (Mantovani et al. 2015) – Bentes et al. (2015) developed an indirect immunofluorescence assay using antigen-specific IgY antibodies. This platform detected viral antigens within frozen liver tissues of experimentally infected monkeys, offering a methodology adaptable to broader diagnostic and research applications.

In addition, an IgY-based diagnostic methodology was developed for enterovirus 71 (EV71), the main etiological agent of hand, foot, and mouth disease, which is transmitted via the fecal–oral route and widely distributed worldwide, primarily affecting children under 5 years of age (Chang et al. 2016; Chen et al. 2007). Following the immunization of chickens with inactivated EV71, the extracted IgY antibodies specifically recognized viral capsid proteins VP2 and VP3. When integrated into a fluorescence sensor platform, these antibodies achieved a detection limit of 10^4 plaque-forming units/ml and demonstrated 94.44% concordance with clinical samples confirmed by RT-PCR (Nie et al. 2019).

Furthermore, Amaral et al. (2025) characterized the production and purification of polyclonal anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) IgY for diagnostic purposes. ELISA and dot blot assays confirmed that IgY effectively detected SARS-CoV-2 in clinical saliva samples, exhibiting high accuracy, sensitivity, specificity, positive and negative predictive values, and strong inter-rater reliability via Cohen's κ coefficient.

In veterinary medicine, Qi et al. (2024) developed an IgY-based ELISA targeting the E2 protein of bovine viral diarrhea virus (BVDV) to detect this specific pathogen among various agents causing diarrhea

in cattle. The assay demonstrated high specificity by exclusively recognizing BVDV. When integrated into immunochromatographic and ELISA platforms, IgY antibodies produced against canine parvovirus-like particles demonstrated high sensitivity and specificity in identifying the virus in canine fecal samples (Wang Z et al. 2020).

Protozoan infection

Silva et al. (2019) used IgY antibodies to develop an epidemiological monitoring model for malaria and leishmaniasis. Chickens exposed to bites from infected mosquitoes produced antigen-specific IgY antibodies targeting both vector saliva and the parasites. These antibodies were subsequently detected in egg yolks using ELISA, establishing a novel methodology for epidemiological surveillance in rural areas.

To advance the diagnosis of malaria – the most important parasitic disease worldwide (World Health Organization 2020) – researchers have increasingly investigated IgY antibodies. Hurdayal et al. (2010) produced IgY antibodies targeting *Plasmodium* lactate dehydrogenase peptides, which effectively identified the native protein in Western blot and immunofluorescence assays. Similarly, IgY antibodies raised against *Plasmodium* glyceraldehyde 3-phosphate dehydrogenase recognized the native protein in ELISA and immunofluorescence assays (Krause et al. 2017).

In parasitology, IgY has been primarily applied to diagnose various diseases, including clonorchiasis, schistosomiasis, and toxoplasmosis (León-Núñez et al. 2022). Chickens immunized with the surface antigen 1 (SAG1) protein of *Toxoplasma gondii* produced specific IgY antibodies with high efficiency and scalability (Cakir-Koc 2016). Cakir-Koc et al. (2020) subsequently coupled these antibodies to latex beads, which successfully recognized cells infected with *T. gondii* tachyzoites in agglutination assays, confirming their diagnostic utility. Similarly, Sert et al. (2017) developed an immunofluorescence assay using fluorescein isothiocyanate-labeled anti-SAG1 IgY, while Júnior et al. (2012) generated anti-soluble tachyzoite antigen IgY antibodies (targeting *T. gondii* tachyzoite proteins) to detect parasitic forms via immunohistochemical analysis of paraffin-embedded tissue sections and cell culture monolayers. Additionally, Ferra et al. (2025) evaluated the diagnostic potential of IgY for detecting *T. gondii* by producing IgY antibodies against SAG1, confirming strong immunoreactivity with the target antigen in ELISA and Western blot assays.

CRISPR-Cas (Clustered Regularly Interspaced Short Palindromic Repeats and CRISPR-associated protein) systems are increasingly applied in molecular diagnostics for highly specific nucleic acid detection. Recently, IgY antibodies targeting *Streptococcus pyogenes* Cas9 (SpCas9) were developed to detect CRISPR-Cas components in biological samples, showing high specificity and sensitivity in *Leishmania braziliensis* promastigotes expressing SpCas9 (León et al. 2023).

Helminth infection

To address diseases caused by nematodes, De Faria et al. (2019) characterized IgY antibodies raised against antigenic extracts of infectious filariform larvae (iL3) and parthenogenetic females (pF) of *Strongyloides venezuelensis*. In ELISA, the antibodies yielded sensitivities of 95.56% and 88.89% and specificities of 95.56% and 91.11% for iL3 and pF, respectively. Based on a similar approach, Teimoori et al. (2017) developed a sandwich ELISA using anti-recombinant *Opisthorchis viverrini* cathepsin F IgY. This assay achieved a detection limit of 70 ng of parasitic antigens, exhibiting an overall specificity and sensitivity of 93.3% and 76.7%, respectively.

Depending on the objective, interspecies cross-reactivity can be leveraged in the development of immunodiagnostics. This was demonstrated by Carrara et al. (2020), who produced IgY antibodies against the hydrophobic fraction of *Taenia crassiceps* metacestodes to diagnose human neurocysticercosis (NCC) – a neglected neurological disease caused by *T. solium*. Using serum-derived *T. crassiceps* as an antigen source circumvents the difficult and invasive extraction of *T. solium* from human cerebrospinal fluid. In a sandwich ELISA, these antibodies demonstrated 93.2% sensitivity and 94.3% specificity when evaluating patients with confirmed NCC, offering a simpler and highly effective diagnostic alternative.

Soil-transmitted helminthiasis is the most prevalent neglected tropical disease (Mutombo et al. 2019). While optical microscopy is the conventional diagnostic standard, its diagnostic accuracy is frequently limited by parasite viability and the technician's experience (Mutombo et al. 2019). To overcome these limitations, Souza et al. (2020) immunized chickens with a saline extract of *Ancylostoma ceylanicum* to isolate IgY antibodies, which were subsequently purified and integrated into

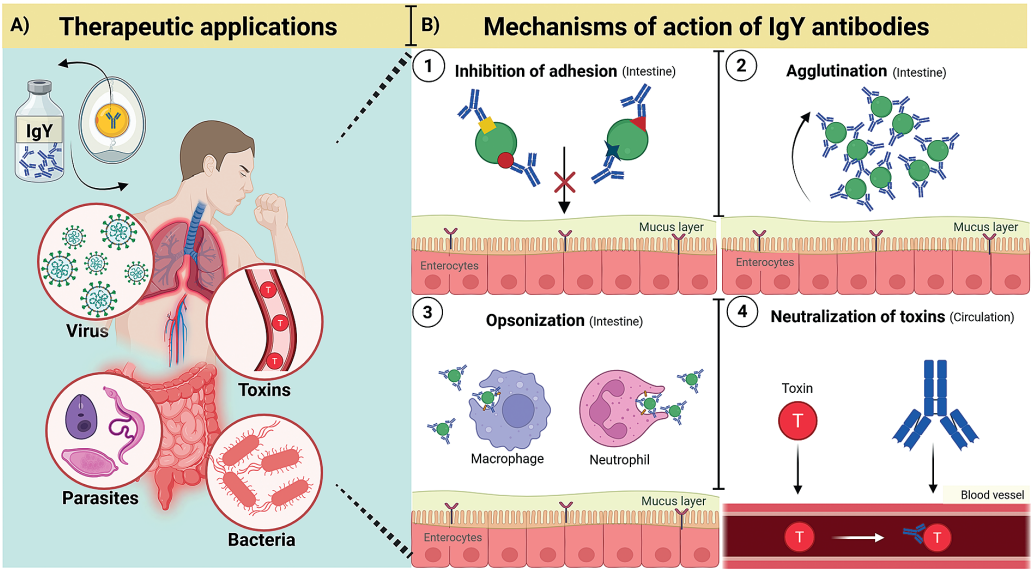

Figure 2. Therapeutic applications and mechanisms of action of immunoglobulin Y (IgY) antibodies. (**A**) Therapeutic potential of IgY against different biological agents. (**B**) Primary mechanisms of action of IgY immunotherapies: (1) inhibition of microbial adhesion to the host epithelium; (2) agglutination of microorganisms, facilitating their clearance; (3) opsonization, promoting their recognition and subsequent phagocytosis by immune cells; and (4) toxin neutralization, blocking their biological effects

a sandwich ELISA to detect protein complexes in serum from infected individuals. The assay achieved 90% sensitivity and 86.7% specificity, demonstrating its potential as a robust alternative to optical microscopy.

Similarly, diagnosing human ascariasis – a disease that primarily affects the poorest regions of the world – is often delayed because *Ascaris* species can take up to 60 days to become detectable in the feces of infected individuals (Bharti et al. 2018). To facilitate early diagnosis, Lopes et al. (2019) developed antibodies against *A. suum* extract and confirmed their recognition of *A. suum* proteins by immunoblotting, which identified 12 distinct protein bands corresponding to the extract, and by immunofluorescence using eggs, uterine portions, and cuticles of *A. suum*. The antibodies showed 80% sensitivity and 90% specificity, establishing a novel, cost-effective tool adaptable to various immunodiagnostic modalities for ascariasis.

Therapeutic applications of IgY antibodies against viral, bacterial, parasitic, and venom targets

IgY antibodies act primarily through antigen-specific recognition and targeted blocking, exerting their therapeutic effects via mechanisms such as microbial adhesion inhibition, pathogen agglutination, and opsonization across different classes of biological agents (Figure 2).

In bacterial targets, IgY binds to structures exposed on the surface of Gram-negative organisms, including fimbriae (pili), flagella, lipopolysaccharides (LPSs), and outer membrane proteins (Zhang et al. 2024). This interaction impairs the function of these components and disrupts signaling pathways associated with colonization, thereby preventing adhesion and inhibiting bacterial growth (Qiu et al. 2025).

During viral infections, IgY inhibits the initial stages of pathogenesis by blocking viral surface proteins from binding to host cell receptors (Artman et al. 2021). In parasites, including protozoa and helminths, IgY interferes with invasion and survival by directly targeting virulence factors and enzymes (Grando et al. 2017; Borges et al. 2018). Furthermore, in antivenom therapy, IgY binds explicitly to toxic venom components, neutralizing their biological activity and reducing their deleterious systemic effects (Leiva et al. 2021; Krishnaraj et al. 2025).

The agglutinating activity of IgY involves microbial aggregation mediated by multivalent epitope binding (Thu et al. 2017). For example, IgY cross-links pathogen cell walls to promote agglutination, thereby inhibiting biofilm formation in *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis* (Li et al. 2020) – key anaerobic bacteria causing periodontal disease.

Additionally, IgY binding to surface antigens enhances phagocytosis of invading microorganisms. Anti-*Pseudomonas* IgY has been demonstrated to promote bacterial opsonization, significantly accelerating the phagocytic activity of human polymorphonuclear neutrophils (Thomsen et al. 2015).

Zhou and Ma (2018) cultured murine peritoneal macrophages and THP-1 cells with anti-LPS IgY *in vivo* and *in vitro*, respectively, and observed that anti-LPS IgY stimulated macrophage proliferation, promoted pseudopod extension, and increased overall phagocytic capacity.

Collectively, IgY antibodies exert protective effects by neutralizing pathogens and toxins, regulating intestinal immunity, and downregulating inflammation or allergic responses. Due to their excellent safety and accessibility, IgY antibodies hold significant potential for mitigating gastrointestinal infections and enhancing mucosal immunity (Qiu et al. 2025).

Passive immunization with IgY antibodies offers a viable alternative for managing infections in immunocompromised individuals while avoiding the adverse effects associated with vaccination. The antibody preparations primarily contain polyclonal IgY isolated from the serum of immunized hosts such as chickens (Abbas et al. 2019).

Furthermore, IgY provides a non-antibiotic strategy for managing infectious diseases, reducing the risk of antimicrobial resistance (El-Kafrawy et al. 2023). Consequently, the commercial integration of IgY-based biotherapeutic products has surged, particularly in dietary supplements and topical applications – such as creams, ointments, gels, and sprays – destined for human use (Yakhkeshi et al. 2025).

The prophylactic and therapeutic efficacy of IgY antibodies against different veterinary viruses has also been extensively studied. Oral administration of IgY exerts protective effects against bovine coronavirus and group A rotavirus in cattle, canine parvovirus and canine distemper virus in dogs, and Newcastle disease virus, influenza, and reovirus in birds (Hridya et al. 2025).

IgY antibodies obtained from the yolk of bird eggs have been tested against infectious, autoimmune, and allergic diseases. In particular, yolk-derived antibodies have been successfully used against viral and bacterial pathogens causing respiratory disorders in humans and animals (León-Núñez et al. 2022). Concurrently, IgY-based antivenoms have demonstrated neutralization capacity against venoms from snakes including *Naja naja*, *Trimeresurus albolabris*, and *Bothrops alternatus* (Capotă et al. 2025).

IgY establishes an effective immunological barrier. Specifically, surface-applied IgY effectively traps pathogens before their host entry inducing passive immunity (Lee et al. 2021), while orally administered IgY neutralizes enteric pathogens – such as *Escherichia coli*, *Clostridium difficile*, *Salmonella*, and rotavirus – by binding toxins or blocking pathogen adhesion.

In addition to infectious diseases, the development of a powdered egg yolk formula with protective sugars containing anti-gliadin IgY showcases the versatility of IgY technology in managing celiac disease. The formulation neutralized both isolated gliadin and gliadin present in the food matrix *in vitro*, which prevented intestinal absorption in mice, presenting a promising prophylactic strategy for celiac disease (Grzywa et al. 2023).

Ultimately, IgY can function as a natural, cost-effective molecule providing passive immunity against a broad spectrum of bacterial, viral, fungal, and parasitic pathogens in humans and animals (Table 1). Intervention with IgY effectively serves as a cocktail therapy by targeting multiple pathogens, allowing clinicians to establish tailored therapeutic regimens based on a comprehensive analysis of the patient's condition (Yakhkeshi et al. 2022).

Although IgY-mediated protection is transient and requires repeated dosing when individuals are at risk of exposure, it delivers immediate effect, unlike vaccines, which require 5–6 weeks to induce protection (Chen et al. 2022).

Antiviral therapy

By targeting specific viral proteins and disrupting host cell attachment, IgY antibodies act as effective agents for preventing and treating viral infections (Tabll et al. 2024). Somasundaram et al. (2020) generated monoclonal IgY using the phage display method, highlighting its potential application as a passive immunotherapeutic strategy against SARS-CoV-2.

Similarly, Ge et al. (2022) used phage display to develop a single-chain variable fragment of IgY (IgY-scFv) that demonstrated significant binding capacity for the S1 fragment of the SARS-CoV-2 spike protein. Their analysis revealed that electrostatic interactions

Table 1. Overview of immunoglobulin Y (IgY)-based therapeutic interventions

Biological agent	*In vivo*/*in vitro* study	Human/animal model	Route of administration	IgY effects	Reference
SARS-CoV-2	*In vitro*	Not applicable	Not applicable	It is anticipated that chicken-derived scFv IgY antibodies developed against SARS-CoV-2 using phage display technology could serve as a potential model for the efficient mass production of high-affinity IgY antibodies to treat this disease, with standardized preparation for effective long-term use.	Somasundaram et al. (2020)
H5N1 (influenza)	*In vivo*	Mice	Intranasal	Protects mice from influenza virus-induced pathology, and the treatment does not inhibit the development of protective immunity after challenge with either heterologous or homologous influenza virus.	Eriksson et al. (2024)
Porphyromonas gingivalis	*In vivo*	Mice and humans	Oral	Protection against dental caries, plaque accumulation, and reinfection.	Xu et al. (2018)
Enterotoxigenic *Escherichia coli*	*In vivo*	Humans	Oral	Reduction in the duration of diarrhea in children whose stools contained one or more target organisms at the time of inclusion in the study.	Gaensbauer et al. (2017)
Deinagkistrodon acutus	*In vivo*	Mice	Subcutaneous	Effective in neutralizing the lethal effects and the hemorrhagic, edematous, and myotoxic activities of *Deinagkistrodon acutus* venom.	Liu et al. (2017)
Pseudomonas aeruginosa	*In vitro*/*in vivo*	Mice	Intravenous	Anti-PAO1 IgY effectively protected burned, infected mice and reduced the bacterial load. Many studies on the therapeutic applications of IgY have consistently shown that, although these antibodies successfully inhibit initial bacterial colonization, they are ineffective in preventing systemic infections.	Ahmadi et al. (2024)
Bovine respiratory syncytial virus (BRSV)	*In vitro*	Not applicable	Not applicable	Preparation of purified IgY, obtained from chickens immunized with BRSV, neutralized BRSV *in vitro*.	Lee et al. (2017)

Table 1. Cont.

Biological agent	*In vivo*/*in vitro* study	Human/animal model	Route of administration	IgY effects	Reference
Mycobacterium tuberculosis (TB)	*In vitro*	Not applicable	Not applicable	Specific IgY against TB increased from two weeks after the first immunization and persisted for 200 days after the last immunization.	Sudjarwo et al. (2017)
Acinetobacter baumannii	*In vivo*	Mice	Intraperitoneal	Anti-*Acinetobacter baumannii* IgY specific for pan-resistant strains reduced inflammatory cytokine levels, pulmonary inflammation, and mortality.	Shi et al. (2017)
Staphylococcus aureus	*In vitro*	Not applicable	Not applicable	The specific IgY showed high binding specificity and inhibited bacterial growth in culture, likely by disrupting interactions with surface antigens, and exhibited no cross-reactivity with other bacterial strains.	Jagadeeswari et al. (2015)
Trypanosoma cruzi	*In vivo*	Mice	Intraperitoneal	IgY treatment reduced parasitemia on day 6 post-infection (PI) compared to the infected control group, but levels were similar by day 8 PI. Additionally, infected and treated animals (groups E and F) showed no amastigotes in cardiac tissue or cardiac lesions compared to the positive control group (group D).	Grando et al. (2018)
Escherichia coli K88	*In vivo*	Pigs	Oral	Complete reduction of *Escherichia coli* 72 hours after challenge.	Wang et al. (2019)
Salmonella enteritis (SE) and *Salmonella typhimurium* (ST)	*In vivo*	Humans	Oral	Significant reduction in *Salmonella* colony counts in the cecum.	Karabasanavar et al. (2022)

SARS-CoV-2 – acute respiratory syndrome coronavirus 2, scFv – single-chain variable fragment.

govern the binding affinity and overall stability of the antibody–antigen complex, suggesting the potential of IgY-scFv in passive immunotherapy and immunoassays.

Schwartz et al. (2022) demonstrated that prophylactic administration of IgY targeting six different *Pseudomonas aeruginosa* strains significantly reduced intravesical bacterial load in a mouse model of *P. aeruginosa*-induced urinary tract infection, suggesting a novel non-antibiotic strategy.

Eriksson et al. (2024) investigated the impact of influenza virus-specific IgY antibodies on host immune responses in adult and elderly immunocompetent mice against adult immunocompromised mice. Prophylactic intranasal administration of anti-H5N1 IgY protected the cohorts against influenza virus-induced symptoms without hindering the development of protective immunity following a viral challenge.

Rotaviruses induce severe gastrointestinal diseases, causing high mortality across various animal species and severe watery diarrhea and vomiting in infants and young children (Lee et al. 2021). In a meta-analysis evaluating 2,626 infants, Wang X et al. (2019) observed significantly superior therapeutic efficacy in those who received oral anti-rotavirus IgY (n = 1,347) compared to those who received conventional treatment (n = 1,279).

IgY-based treatment has also been explored for Ebola virus infections, which cause high mortality rates in humans and nonhuman primates (World Health Organization 2021). Zhang Y et al. (2021) evaluated anti-Ebola virus IgY in neonatal mice and confirmed that high-dose administration conferred complete protection, whereas the low-dose group exhibited partial protection.

Antibacterial therapy

Because bacteria can self-replicate and secrete virulence factors to colonize host cells and tissues, IgY is an effective therapeutic tool to reduce and prevent bacterial colonization (León-Núńez et al. 2022).

Specific IgY antibodies have been used against several oral pathogens, including *Streptococcus mutans* and *P. gingivalis*. Studies have shown that these antibodies can inhibit dental caries progression, plaque accumulation, and reinfection (Xu et al. 2018). To counter other oral pathologies such as periodontitis and halitosis, Wang F et al. (2019) evaluated the ability of IgY to inhibit the growth of *Fusobacterium nucleatum* cultured in tubes containing different concentrations of the antibody, demonstrating dose-dependent bacterial suppression.

IgY antibody-based treatment has also been extensively studied for *E. coli*, a key member of mammalian microflora, with several pathotypes associated with enteric diseases. In a randomized, placebo-controlled trial, Gaensbauer et al. (2017) administered a combined IgY preparation (PTM202) targeting rotavirus, enterotoxigenic *E. coli*, Shiga-positive *E. coli*, and *Salmonella* or a placebo for 3 days to 301 Guatemalan children presenting with acute non-bloody diarrhea. Among children with confirmed infections from one or more target pathogens, PTM202 treatment significantly shortened the duration of diarrheal episodes compared to the placebo.

To combat MBTC, which is responsible for tuberculosis – a fatal respiratory disease characterized by extrapulmonary manifestations and increasing mortality due to antibiotic resistance (Chauhan et al. 2021) – Sudjarwo et al. (2017) used a rat peripheral blood mononuclear cell model and demonstrated that high-dose administration of anti-MBTC IgY significantly upregulated interleukin-2 expression. The use of IgY may also hold promise for managing nontuberculous mycobacterial pulmonary infections, which remain clinically challenging due to widespread antimicrobial intolerance and drug resistance (Shulha et al. 2019).

Furthermore, Rezaeifard et al. (2021) investigated diphtheria, a bacterial disease caused by the cytotoxin secreted by *Corynebacterium diphtheriae*. A cell culture assay evaluating the neutralizing activity of anti-diphtheria toxin (anti-DT) IgY demonstrated that these antibodies effectively neutralized the toxin, offering an alternative to conventional equine-derived antibodies. Subsequent *in vivo* assessments also validated the neutralizing effect of anti-DT IgY, providing compelling evidence of its potential therapeutic use.

Antiparasitic therapy

Sampaio et al. (2014) generated high-avidity IgY antibodies against the protozoan *Trypanosoma evansi*. While the antibodies exhibited no prophylactic effect or infection control in treated mice, administering anti-*T. evansi* IgY significantly prolonged survival rates when used in combination with anti-hematozoan drugs.

Grando et al. (2017) immunized chickens with *T. cruzi* trypomastigotes and extracted anti-*T. cruzi* IgY, which demonstrated cross-reactivity with *T. evansi* antigens in

a Western blot assay. Although the authors concluded that anti-*T. cruzi* IgY lacks specificity as a diagnostic tool, *T. cruzi* antigens can effectively control infection and reduce disease progression, thus serving as a form of therapeutic immunization or immunotherapy.

In a subsequent study, Grando et al. (2018) demonstrated in a murine model that prophylactic administration of anti-*T. cruzi* IgY at 50 mg/kg reduced post-challenge parasitemia and prevented the development of amastigote-induced cardiac lesions. Notably, therapeutic administration of the same dosage yielded identical protective effects, while concurrently improving the immune response by suppressing aberrant enzyme activity in the splenic lymphocytes of the animals.

Furthermore, Hashemzadeh Farhang and Shahbazi (2016) evaluated IgY as a potential agent against *Cryptosporidium* infection. *In vitro*, IgY antibodies produced against *C. parvum* oocyst antigens exhibited high specificity, significantly impairing parasite binding to Caco-2 cells, and neutralized *C. parvum* viability.

Antivenom therapy

In recent years, eggs from antigen-immunized hens have emerged as a valuable source of IgY antibodies. Numerous studies on snake IgY antivenoms have confirmed that yolk-derived IgY represents a promising alternative to conventional antivenoms produced in large mammalian hosts, such as horses (Liu et al. 2017).

A primary clinical limitation of antivenoms produced in animals such as goats, sheep, and horses is the high incidence of hypersensitivity reactions triggered by residual serum proteins resulting from insufficient IgG purification. Because IgY can be readily purified, its use may significantly minimize these adverse effects (Pereira et al. 2019).

Da Rocha et al. (2017) produced IgY antibodies against venom toxins of *Crotalus durissus terrificus*, *Bothrops jararaca*, and *Bitis arietans*. Western blot assays confirmed that these antibodies bound to specific venom components, while *in vivo* assays demonstrated IgY harvested after the ninth immunization conferred 100% protection in envenomed mice. Similarly, Duan et al. (2016) isolated antivenom IgY from the eggs of hens immunized with *Trimeresurus albolabris* venom. The antibodies recognized most venom proteins in Western blot analyses and dose-dependently neutralized their toxic effects in mice.

Limitation and challenges in the use of IgY technology

Despite its potential, the widespread application of IgY technology in diagnostics and therapy faces important limitations. IgY does not activate the mammalian complement system or bind Fc receptors, which makes it an ideal agent for *in vitro* applications (Constantin et al. 2020). However, the lack of these interactions raises questions regarding its efficacy and safety in systemic applications, requiring further investigation (Esmaeili et al. 2025).

From a therapeutic perspective, oral administration presents significant challenges due to the high susceptibility of IgY to degradation under physiological conditions. Within the gastrointestinal tract, the antibody undergoes rapid degradation by proteolytic enzymes – including pepsin, trypsin, chymotrypsin, and elastase – highlighting the need for advanced gastroprotective strategies such as encapsulation (Wang H et al. 2023).

Additional limitations are associated with antibody production. Recombinant monoclonal IgY offers high specificity but is limited by elevated production costs, complex epitope identification, and lengthy development timelines (Tabll et al. 2024). In contrast, polyclonal IgY preparations exhibit batch-to-batch variability due to differences in antibody composition and antibody affinity among hens, necessitating rigorous validation and analytical characterization (Leow et al. 2021).

In diagnostics, a major barrier to regulatory approval and scalability is the lack of standardized protocols for the use of specific pathogen-free animals and production, extraction, and purification processes (Lee et al. 2021). Furthermore, restrictive intellectual property protection has deterred interest and investment in the commercial development of IgY-based products (Yakhkeshi et al. 2022).

Notably, many applications utilize IgY antibodies in the form of crude extracts, which do not have a high level of purity. However, for broad application in diagnostics and therapies and large-scale commercialization, it is essential to thoroughly characterize the composition of IgY products and evaluate their safety for use in humans and animals (Zhang et al. 2023).

Finally, although IgY is generally considered safe, its long-term effects remain poorly characterized, particularly in children and immunocompromised individuals (Esmaeili et al. 2025). Even highly purified preparations may harbor residual egg proteins capable of triggering

hypersensitivity reactions in susceptible populations (El-Kafrawy et al. 2026). Therefore, extensive clinical studies are required to evaluate potential antigenic and allergic responses (Lee et al. 2021).

Ultimately, overcoming these challenges will depend on coordinated basic and applied research, optimization of production processes, and the development of clear regulatory frameworks. Implementing these steps is essential to ensure product quality and reproducibility, and expand clinical validation of efficacy and safety of IgY-based platforms for diagnostic and therapeutic applications (El-Kafrawy et al. 2026).

Conclusions

Egg yolk IgY-based technology shows promising potential for advancing diagnostics and therapeutics, distinguished by its high specificity, cost-effective production, and reduced risk of cross-reactivity with human proteins.

Immunoassays employing IgY have consistently demonstrated high sensitivity and accuracy in the detection of pathogens, disease biomarkers, and toxins – thereby facilitating rapid and reliable diagnostics. In the therapeutic field, IgY antibodies represent an innovative and safe alternative to conventional drugs, given the growing concern over antimicrobial resistance and adverse effects.

Although challenges persist regarding protocol standardization, production scalability, and regulatory approval frameworks, the growing body of scientific evidence validates IgY as a viable strategy for the future of diagnostic and therapeutic medicine, capable of improving both human and animal health.

Acknowledgments

We would like to thank the institutions Fundação de Amparo á pesquisa do Amazonas – FAPEAM, EDITAL N. 004/2024 – PEX-CT&I/FAPEAM, Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – CAPES (Bolsista CAPES Brasil), and Conselho Nacional de Desenvolvimento Científico e Tecnológico – CNPq for the financial support awarded to this study.

Conflicts of interest

The authors declare that they have no conflict of interest.

Ethical approval

Ethics committee approval was not required for this study.

Author contributions

L.C.C. and J.C.G. collected and assembled the data. J.C.G. and L.A.M.M. conceived and designed the study. L.C.C., J.C.G., and C.C.S. analyzed and interpreted the data. L.C.C., J.C.G., J.V.M.S., J.M.G., and L.A.M.M. wrote the manuscript. L.C.C., J.C.G., C.C.S., J.V.M.S., and L.A.M.M. critically revised the manuscript. L.C.C., J.C.G., C.C.S., J.V.M.S., and L.A.M.M. approved the final version. All authors read and approved the final manuscript.

References

Abbas AT, El-Kafrawy SA, Sohrab SS, Azhar EIA. 2019. IgY antibodies for the immunoprophylaxis and therapy of respiratory infections. Hum Vaccin Immunother. 15: 264–275. https://doi.org/10.1080/21645515.2018.1514224.

Ahmadi TS, Behrouz B, Mousavi Gargari SL. 2024. Polyclonal anti-whole cell IgY passive immunotherapy shields against *P. aeruginosa*-induced acute pneumonia and burn wound infections in murine models. Sci Rep. 14: 405. https://doi.org/10.1038/s41598-023-50859-x.

Amaral CML, Júnior VCP, Lima DF, Costa HPS, Farias DAB, Neto JXS, Moura LFWG, Silva BB, Freitas ER, Tilburg MFV, Guedes MIF. 2025. Utilização de IgY para diagnóstico de infecções respiratórias: aplicação prática em COVID-19. Future Sci OA. 11: 2546245. https://doi.org/10.1080/20565623.2025.2546245.

Amro WA, Al-Qaisi W, Al-Razem F. 2018. Production and purification of IgY antibodies from chicken egg yolk. J Genet Eng Biotechnol. 16: 99–103. https://doi.org/10.1016/j.jgeb.2017.10.003.

Artman C, Brumfield KD, Khanna S, Goepp J. 2021. Avian antibodies (IgY) targeting spike glycoprotein of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) inhibit receptor binding and viral replication. PLoS One 16: e0252399. https://doi.org/10.1371/journal.pone.0252399.

Azman AS, Moore SM, Lessler J. 2020. Surveillance and the global fight against cholera: setting priorities and tracking progress. Vaccine 38(Suppl 1): A28–A30. https://doi.org/10.1016/j.vaccine.2019.06.037.

Bayat M, Khabiri A, Hemati B. 2018. Development of IgY-based sandwich ELISA as a robust tool for rapid detection and discrimination of toxigenic *Vibrio cholerae*. Can J Infect Dis Med Microbiol. 2018: 4032531. https://doi.org/10.1155/2018/4032531. Erratum in: Can J Infect Dis Med Microbiol. 2019; 2019: 4164982. https://doi.org/10.1155/2019/4164982.

Bentes GA, Lanzarini NM, Lima LR, Manso PP, da Silva Ados S, Mouta Junior Sda S, Guimarães JR, de Moraes MT, Pelajo-Machado M, Pinto MA. 2015. Using immunoglobulin Y as an alternative antibody for the detection of hepatitis A virus in frozen liver sections. Mem Inst Oswaldo Cruz. 110: 577–579. https://doi.org/10.1590/0074-02760140457.

Bharti B, Bharti S, Khurana S. 2018. Worm infestation: diagnosis, treatment and prevention. Indian J Pediatr. 85: 1017–1024. https://doi.org/10.1007/s12098-017-2505-z.

Bizanov G. 2017. IgY extraction and purification from chicken egg yolk. J Hellenic Vet Med Soc. 68: 265–272.

Borges IP, Silva MF, Santiago FM, Faria LS, Júnior AF, Silva RJ, Costa MS, Freitas V, Yoneyama KAG, Ferro EAV, et al. 2018. Antiparasitic effects induced by polyclonal IgY antibodies anti-phospholipase A2 from *Bothrops pauloensis* venom. Int J Biol Macromol. 112: 333–342. https://doi.org/10.1016/j.ijbiomac.2018.01.178.

Bouvard V, Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, et al. 2009. A review of human carcinogens – Part B: biological agents. Lancet Oncol 10: 321–322. https://doi.org/10.1016/s1470-2045(09)70096-8.

Budama-Kilinc Y, Cakir-Koc R, Ozdemir B, Kaya Z, Badur S. 2018. Production and characterization of a conserved M2e peptide-based specific IgY antibody: evaluation of the diagnostic potential via conjugation with latex nanoparticles. Prep Biochem Biotechnol. 48: 930–939. https://doi.org/10.1080/10826068.2018.1525564.

Cakir-Koc R. 2016. Production of anti-SAG1 IgY antibody against *Toxoplasma gondii* parasites and evaluation of antibody activity by ELISA method. Parasitol Res. 115: 2947-2952. https://doi.org/10.1007/s00436-016-5047-9.

Cakir-Koc R, Budama-Kilinc Y, Ustun E, Babur C. 2020. Conjugation and characterization of latex particles with *Toxoplasma gondii*-specific immunoglobulin Y antibodies for diagnostic aim and evaluation efficiency in in vitro culture. J Equine Vet Sci. 92: 103145. https://doi.org/10.1016/j.jevs.2020.103145.

Capotă R, Ciauşu-Sliwa D, Bostănaru-Iliescu AC, Năstasă V, Mareş M. Latest findings in immunoglobulin Y technologies and applications. Int J Mol Sci. 2025; 26: 6380. https://doi.org/10.3390/ijms26136380.

Carrara GMP, Silva GB, Faria LS, Nunes DS, Ribeiro VS, Lopes CA, Gonçalves-Pires MDRF, Santos MM, Borges IP, Ferreira-Junior Á, et al. 2020. IgY antibody and human neurocysticercosis: a novel approach on immunodiagnosis using *Taenia crassiceps* hydrophobic antigens. Parasitology 147: 240–247. https://doi.org/10.1017/S0031182019001446.

Chang PC, Chen SC, Chen KT. 2016. The current status of the disease caused by Enterovirus 71 infections: epidemiology, pathogenesis, molecular epidemiology, and vaccine development. Int J Environ Res Public Health 13: 890. https://doi.org/10.3390/ijerph13090890.

Chauhan A, Kumar M, Kumar A, Kanchan K. 2021. Comprehensive review on mechanism of action, resistance and evolution of antimycobacterial drugs. Life Sci. 274: 119301. https://doi.org/10.1016/j.lfs.2021.119301.

Chen CJ, Hudson AF, Jia AS, Kunchur CR, Song AJ, Tran E, Fisher CJ, Zanchi D, Lee L, Kargotich S, et al. 2022. Affordable IgY-based antiviral prophylaxis for resource-limited settings to address epidemic and pandemic risks. J Glob Health 12: 05009. https://doi.org/10.7189/jogh.12.05009.

Chen KT, Chang HL, Wang ST, Cheng YT, Yang JY. 2007. Epidemiologic features of hand-foot-mouth disease and herpangina caused by enterovirus 71 in Taiwan, 1998–2005. Pediatrics 120: e244–e252. https://doi.org/10.1542/peds.2006-3331.

Chen W, Kim JH, Zhang D, Lee KH, Cangelosi GA, Soelberg SD, Furlong CE, Chung JH, Shen AQ. 2013. Microfluidic one-step synthesis of alginate microspheres immobilized with antibodies. J R Soc Interface. 10: 20130566. https://doi.org/10.1098/rsif.2013.0566.

Conroy PJ, Law RH, Caradoc-Davies TT, Whisstock JC. 2017. Antibodies: from novel repertoires to defining and refining the structure of biologically important targets. Methods 116: 12–22. https://doi.org/10.1016/j.ymeth.2017.01.003.

Constantin C, Neagu M, Supeanu TD, Chiurciu V, Spandidos DA. 2020. IgY – turning the page toward passive immunization in COVID-19 infection (review). Exp Ther Med. 20: 151–158. https://doi.org/10.3892/etm.2020.8704.

Da Rocha DG, Fernandez JH, De Almeida CMC, Da Silva CL, Magnoli FC, Da Silva OÉ, Da Silva WD. 2017. Development of IgY antibodies against anti-snake toxins endowed with highly lethal neutralizing activity. Eur J Pharm Sci. 106: 404–412. https://doi.org/10.1016/j.ejps.2017.05.069.

De Faria LS, de Souza DLN, Ribeiro RP, de Sousa JEN, Borges IP, Ávila VMR, Ferreira-Júnior Á, Goulart LR, Costa-Cruz JM. 2019. Highly specific and sensitive anti-*Strongyloides venezuelensis* IgY antibodies applied to the human strongyloidiasis immunodiagnosis. Parasitol Int. 72: 101933. https://doi.org/10.1016/j.parint.2019.101933.

Duan HL, He QY, Zhou B, Wang WW, Li B, Zhang YZ, Deng QP, Zhang YF, Yu XD. 2016. Anti-*Trimeresurus albolabris* venom IgY antibodies: preparation, purification and neutralization efficacy. J Venom Anim Toxins Incl Trop Dis. 22: 23. https://doi.org/10.1186/s40409-016-0078-3.

El-Kafrawy SA, Abbas AT, Abdel-Dayem UA, El-Kafrawy MS, Azhar EI. 2026. IgY passive immunotherapy for pandemic preparedness: a One Health platform approach against pathogen X. Clin Microbiol Rev. e00249–25. https://doi.org/10.1128/cmr.00249-25.

El-Kafrawy SA, Abbas AT, Oelkrug C, Tahoon M, Ezzat S, Zumla A, Azhar EI. 2023. IgY antibodies: the promising potential to overcome antibiotic resistance. Front Immunol. 14: 1065353. https://doi.org/10.3389/fimmu.2023.1065353.

Eriksson M, Nylén S, Grönvik KO. 2024. Passive immunization of mice with IgY anti-H5N1 protects against experimental influenza virus infection and allows development of protective immunity. Vaccine 42: 126133. https://doi.org/10.1016/j.vaccine.2024.07.034.

Esmaeili Z, Kamal Shahsavar S, Ghazvini K. 2025. A systematic review of the avian antibody (IgY) therapeutic effects on human bacterial infections over the decade. Antib Ther. 8: 111–123. https://doi.org/10.1093/abt/tbaf007.

Ferra BT, Hadaś E, Jankowska K, Golab E, Dziadek B. 2025. Development of *Toxoplasma gondii* recombinant chimeric proteins as potential alternatives to whole-cell tachyzoite lysate in serodiagnosis. Int J Mol Sci. 26: 4384. https://doi.org/10.3390/ijms25084384.

Ferreira-Júnior Á, Santiago FM, Silva MV, Ferreira FB, Macędo Júnior AG, Mota CM, Faria MS, Silva Filho HH, Silva DAO, Cunha-Júnior JP, et al. 2012. Production, characterization and applications for *Toxoplasma gondii*-specific polyclonal chicken egg yolk immunoglobulins. PLoS One 7: 1–10. https://doi.org/10.1371/journal.pone.0040391.

Gaensbauer JT, Melgar MA, Calvimontes DM, Lamb MM, Asturias EJ, Contreras-Roldan IL, Dominguez SR, Robinson CC, Berman S. 2017. Efficacy of a bovine colostrum and egg based intervention in acute childhood diarrhoea in Guatemala: a randomised, double-blind, placebo-controlled trial. BMJ Glob Health 2: e000452. https://doi.org/10.1136/bmjgh-2017-000452.

Ge S, Dias ACP, Zhang X. 2024. Chimerism of avian IgY-scFv and truncated IgG-Fc: a novel strategy in cross-species antibody generation and enhancement. Immunology 172: 46–60. https://doi.org/10.1111/imm.13752.

Ge S, Wu R, Zhou T, Liu X, Zhu J, Zhang X. 2022. Specific anti-SARS-CoV-2 S1 IgY-scFv is a promising tool for recognition of the virus. AMB Express. 12: 18. https://doi.org/10.1186/s13568-022-01355-4.

Grando TH, Baldissera MD, de Sá MF, do Carmo GM, Porto BCZ, Aguirre GSV, Azevedo MI, de Jesus FPK, Santurio JM, Sagrillo MR, et al. 2017. Avian antibodies (IgY) against *Trypanosoma cruzi*: purification and characterization studies. J Immunol Methods 449: 56–61. https://doi.org/10.1016/j.jim.2017.07.002.

Grando TH, Baldissera MD, Do Carmo G, Oliveira CB, Santi ET, Doleski PH, Leal DBR, Stefani LM, Mendes RE, Da Silva AS, et al. 2018. Ecto-enzymes activities in splenic lymphocytes of mice experimentally infected by *Trypanosoma cruzi* and treated with specific avian immunoglobulins: an attempt to improve the immune response. Mol Cell Biochem. 448: 9–15. https://doi.org/10.1007/s11010-018-3308-x.

Grzywa R, Łupicka-Słowik A, Sieńczyk M. 2023. IgYs: on her majesty's secret service. Front Immunol. 14: 1199427. https://doi.org/10.3389/fimmu.2023.1199427.

Haese N, Brocato RL, Henderson T, Nilles ML, Kwilas SA, Josleyn MD, Hammerbeck CD, Schiltz J, Royals M, Ballantyne J, et al. Antiviral biologic produced in DNA vaccine/goose platform protects hamsters against hantavirus pulmonary syndrome when administered post-exposure. PLoS Negl Trop Dis. 9: e0003803. https://doi.org/10.1371/journal.pntd.0003803.

Hashemzadeh Farhang H, Shahbazi P. 2016. Produção de anticorpo específico da gema do ovo (Igy) contra oocistos de *Cryptosporidium parvum*. Med Lab J. 10: 38–42.

Hridya ML, Jogi HR, Revathi A, Thakur R, Patel J, Yadav AK, Bhatt M, Rai V, Upmanyu V, Singh V, Rajak K. 2025. Harnessing the potential of IgY: a creative approach for immunodiagnosis and immunotherapy against viral diseases of animals. Curr Microbiol. 82: 537. https://doi.org/10.1007/s00284-025-04531-4.

Hurdayal R, Achilonu I, Choveaux D, Coetzer THT, Goldring JPD. 2010. Anti-peptide antibodies differentiate between plasmodial lactate dehydrogenases. Peptides 31: 525–532. https://doi.org/10.1016/j.peptides.2010.01.002.

Innes EA, Bartley PM, Buxton D, Katzer F. 2009. Ovine toxoplasmosis. Parasitology 136: 1887–1894. https://doi.org/10.1017/S0031182009991636.

Jagadeeswari M, Dhanabalan R, Saranya G. 2015. Detection of *Staphylococcus aureus* from clinical and sub-clinical bovine mastitis milk samples using chicken egg yolk antibodies (IgY). Int J Appl Pure Sci Agriculture 1: 56–63.

Karabasanavar N, Chakkodabail Benakabhat M, Agalagandi Gopalakrishna S, Bagalkote PS, Basayya Hiremath J, Shivanagowda Patil G, Krishnan Sivaraman G, Barbuddhe BS. 2022. Polyclonal hen egg yolk antibodies could confer passive protection against *Salmonella* serotypes in broiler chicks. J Food Saf 42: e12987. https://doi.org/10.1111/jfs.12987.

Karlsson M, Kollberg H, Larsson A. 2004. Chicken IgY: utilizing the evolutionary advantage. Worlds Poult Sci J. 60: 341–348. https://doi.org/10.1079/wps200422.

Klemperer F. 1893. Über natürliche Immunität und ihre Verwerthung für Immunisirungstherapie. Arch Exp Path Pharmak. 31: 356–382.

Kota RK, Reddy PN, Sreerama K. 2020. Application of IgY antibodies against staphylococcal protein A (SpA) of *Staphylococcus aureus* for detection and prophylactic functions. Appl Microbiol Biotechnol. 104: 9387–9398. https://doi.org/10.1007/s00253-020-10912-5.

Krause RGE, Hurdayal R, Choveaux D, Przyborski JM, Coetzer THT, Goldring JPD. 2017. Glyceraldehyde-3-phosphate dehydrogenase of *Plasmodium*: a potential target for malaria diagnosis. Exp Parasitol. 179: 7–19. https://doi.org/10.1016/j.exppara.2017.05.007.

Krishnaraj PN, Mudnakudu-Nagaraju KK, Prasad N, Venkatesh C, Ramesh D, Venktesh D, Chikkamandagere Kumar A, Ramanna KJ. 2025. Neutralization of systemic toxicity of *Daboia russelii* venom and reprotoxin fraction by IgY antibodies. Med Drug Discov. 100217. https://doi.org/10.1016/j.medidd.2025.100217.

Lee B, Kim HS, Han SY, Jung YT. 2017. Chicken egg yolk antibodies against bovine respiratory syncytial virus neutralize the virus *in vitro*. Acta Virol 61: 115–118.

Lee L, Samardzic K, Wallach M, Frumkin LR, Mochly-Rosen D. 2021. Immunoglobulin Y for potential diagnostic and therapeutic applications in infectious diseases. Front Immunol. 12: 696003. https://doi.org/10.3389/fimmu.2021.696003.

Leiva CL, Gallardo MJ, Casanova N, Terzolo H, Chacana P. 2020. IgY-technology (egg yolk antibodies) in human medicine: a review of patents and clinical trials. Int Immunopharmacol. 81: 106269. https://doi.org/10.1016/j.intimp.2020.106269.

Leiva CL, Geoghegan P, Lammer M, Cangelosi A, Mariconda V, Celi AB, Brero ML, Chacana P. 2021. *In vivo* neutralization of bee venom lethality by IgY antibodies. Mol Immunol. 135: 183–190. doi: 10.1016/j.molimm.2021.04.015.

León E, Ortiz V, Pérez A, Téllez J, Díaz GJ, Ramírez HMH, Contreras RLE. 2023. Anti-SpCas9 IgY polyclonal antibodies production for CRISPR research use. ACS Omega 8: 33809–33818. https://doi.org/10.1021/acsomega.3c04273.

León-Núñez D, Vizcaíno-López MF, Escorcia M, Correa D, Pérez-Hernández E, Gómez-Chávez F. IgY Antibodies as biotherapeutics in biomedicine. Antibodies (Basel) 2022; 11: 62. https://doi.org/10.3390/antib11040062.

Leow CH, et al. 2021. IgY-technology: production and application of egg yolk antibodies: basic knowledge for a successful practice. Cham: Springer. 173–193.

Li X, He P, Yu L, He Q, Jia C, Yang H, Lu M, Wei X, Zhao S. 2020. Production and characteristics of a novel chicken egg yolk antibody (IgY) against periodontitis-associated pathogens. J Oral Microbiol. 12: 1831374. https://doi.org/10.1080/20002297.2020.1831374.

Li X, Wang L, Zhen Y, Li S, Xu Y. 2015. Chicken egg yolk antibodies (IgY) as non-antibiotic production enhancers for use in swine production: a review. J Anim Sci Biotechnol 6: 40. https://doi.org/10.1186/s40104-015-0038-8.

Liu J, He Q, Wang W, Zhou B, Li B, Zhang Y, Luo C, Chen D, Tang J, et al. 2017. Preparation and neutralization efficacy of IgY antibodies raised against *Deinagkistrodon acutus* venom. J Venom Anim Toxins Incl Trop Dis. 23: 22. https://doi.org/10.1186/s40409-017-0112-0.

Lopes CA, de Faria LS, de Sousa JEN, Borges IP, Ribeiro RP, Bueno LL, Rodrigues Ávila VM, Ferreira Júnior Á, Costa-Cruz JM. 2019. Anti-*Ascaris suum* immunoglobulin Y as

a novel biotechnological tool for the diagnosis of human ascariasis. J Helminthol. 94: e71. https://doi.org/10.1017/S0022149X19000701.

Lv T, Xie X, Diao L, Jiang S, Ding Y, Yuan X, Gong L, Chen X, Zhang W, Cao Y. Leptospira-specific immunoglobulin Y (IgY) is protective in infected hamsters. Vaccine 2024; 42: 3220–3229. https://doi.org/10.1016/j.vaccine.2024.04.010.

Mantovani SAS, Delfino BM, Martins AC, Oliart-Guzmán H, Pereira TM, Branco FLCC, Brańa AM, Filgueira-Júnior JA, Santos AP, Arruda RA, et al. 2015. Socioeconomic inequities and hepatitis A virus infection in Western Brazilian Amazonian children: spatial distribution and associated factors. BMC Infect Dis. 15: 428. doi: 10.1186/s12879-015-1164-9.

Michelchen S, Micheel B, Hanack K. 2020. *In vitro* immunization approach to generate specific murine monoclonal IgG antibodies. bioRxiv. https://doi.org/10.1101/2020.11.24.393728.

Moosavi M, Rahimi S, Karimi Torshizi MA, Zahraei Salehi T, Ashrafi Tamai I, Grimes J. 2025. *In vitro* evaluation of the inhibitory potential of specific egg yolk antibodies induced by different antigens of *Salmonella typhimurium*. Poult Sci. 104: 105934. https://doi.org/10.1016/j.psj.2025.105934.

Mudili V, Makam SS, Sundararaj N, Siddaiah C, Gupta VK, Rao PVL. 2015. A novel IgY-Aptamer hybrid system for cost-effective detection of SEB and its evaluation on food and clinical samples. Sci Rep. 5: 15151. https://doi.org/10.1038/srep15151.

Mutombo PN, Man NWY, Nejsum P, Ricketson R, Gordon CA, Robertson G, Clements ACA, Chacón-Fonseca N, Nissapatorn V, Webster JP, et al. 2019. Diagnosis and drug resistance of human soil-transmitted helminth infections: a public health perspective. Adv Parasitol. 104: 247–326. https://doi.org/10.1016/bs.apar.2019.02.004.

Najdi S, Nikbakht Brujeni G, Sheikhi N, Chakhkar S. 2016. Development of anti-*Helicobacter pylori* immunoglobulins Y (IgYs) in quail. Iran J Vet Res. 17: 106–110.

Nie W, Zhao C, Guo X, Sun L, Meng T, Liu Y, Song X, Xu K, Wang J, Li J. 2019. Preparation and identification of chicken egg yolk immunoglobulins against human enterovirus 71 for diagnosis of hand-foot-and-mouth disease. Anal Biochem. 573: 44–50. https://doi.org/10.1016/j.ab.2019.02.029.

Ozkan B, Budama-Kilinc Y, Cakir-Koc R, Mese S, Badur S. Application of an immunoglobulin Y-alkaline phosphatase bioconjugate as a diagnostic tool for influenza A virus. Bioengineered 2019; 10: 33–42. https://doi.org/10.1080/21655979.2019.1586054.

Pacheco BLB, Nogueira CP, Venancio EJ. 2023. IgY antibodies from birds: a review on affinity and avidity. Animals (Basel) 13: 3130. https://doi.org/10.3390/ani13193130.

Pauly D, Chacana PA, Calzado EG, Brembs B, Schade R. 2011. IgY technology: extraction of chicken antibodies from egg yolk by polyethylene glycol (PEG) precipitation. J Vis Exp. 51: 3084. https://doi.org/10.3791/3084.

Pereira EPV, van Tilburg MF, Florean EOPT, Guedes MIF. 2019. Egg yolk antibodies (IgY) and their applications in human and veterinary health: a review. Int Immunopharmacol 73: 293–303. https://doi.org/10.1016/j.intimp.2019.05.015.

Qi S, Wang J, Le T, Sun C, Chang J, Jiang Z, Yin X, Pang Q. 2024. Development of a pan-genotypic monoclonal antibody-based competitive ELISA for the detection of antibodies against bovine viral diarrhea virus. Front Immunol 15: 1504115. https://doi.org/10.3389/fimmu.2024.1504115.

Qiu H, Jin X, Zhang X, Chen K, Wang L, Huang J. 2025. Egg yolk immunoglobulins (IgY) purification, activity enhancement, and potential benefits for human health. Nutrients 17: 2890. https://doi.org/10.3390/nu17172890.

Rezaeifard M, Solhi R, Mohammadi M, Abbasi E, Aminian M. 2021. Production of IgY polyclonal antibody against diphtheria toxin and evaluation of its neutralization effect by Vero cell assay. BMC Biotechnol. 21: 34. https://doi.org/10.1186/s12896-021-00694-7.

Sampaio LC, Baldissera MD, Grando TH, Gressler LT, Capeleto DM, de Sa MF, de Jesus FP, dos Santos AG Jr, Anciuti AN, Colonetti K, et al. 2014. Production, purification and therapeutic potential of egg yolk antibodies for treating *Trypanosoma evansi* infection. Vet Parasitol. 204: 96–103. https://doi.org/10.1016/j.vetpar.2014.05.032.

Schade R, Calzado EG, Sarmiento R, Chacana PA, Porankiewicz-Asplund J, Terzolo HR. 2005. Chicken egg yolk antibodies (IgY-technology): a review of progress in production and use in research and human and veterinary medicine. Altern Lab Anim. 33: 129–154. https://doi.org/10.1177/026119290503300208.

Schade R, Hlinak A. 1996. Egg yolk antibodies, state of the art and future prospects. ALTEX 13: 5–9.

Schwartz FA, Christophersen L, Thomsen K, Baekdal S, Pals Bendixen M, Jřrgensen M, Bull Rasmussen IK, Laulund AS, Hřiby N, et al. 2022. Chicken IgY reduces the risk of *Pseudomonas aeruginosa* urinary tract infections in a murine model. Front Microbiol. 13: 988386. https://doi.org/10.3389/fmicb.2022.988386.

Sert M, Cakir Koc R, Budama Kilinc Y. 2017. Novo anticorpo IgY marcado com FITC: imagem de fluorescęncia de *Toxoplasma gondii in vitro*. Sci Rep. 7: 852. https://doi.org/10.1038/s41598-017-00930-1.

Shi H, Zhu J, Zou B, Shi L, Du L, Long Y, Wang H, Xu H, Zhen Y, Sun L. 2017. Effects of specific egg yolk immunoglobulin on pan-drug-resistant Acinetobacter baumannii. Biomed Pharmacother. 95: 1734–1742. https://doi.org/10.1016/j.biopha.2017.09.112.

Shulha JA, Escalante P, Wilson JW. 2019. Pharmacotherapy approaches in nontuberculous mycobacteria infections. Mayo Clin Proc. 94: 1567–1581. https://doi.org/10.1016/j.mayocp.2018.12.011.

Silva ROE, Almeida MEM, Marialva EF, Balieiro AADS, Castro DP, Rios-Velasquez CM, Mariúba LAM, Pessoa FAC. 2019. Chicken eggs as a surveillance tool for malaria and leishmaniasis vector presence. Rev Soc Bras Med Trop. 52: e20180415. https://doi.org/10.1590/0037-8682-0415-2018.

Sivaprasad MS, Vinod VK, Jisna KS, Nair PM, Parmar N. 2020. Egg yolk (IgY) and its relevance in animal and human health – an updated review. J Food Animal Sci 1: 81–86. https://doi.org/10.51128/jfas.2020.A015

Somasundaram R, Choraria A, Antonysamy M. 2020. An approach towards development of monoclonal IgY antibodies against SARS-CoV-2 spike protein (S) using phage display

method: a review. Int Immunopharmacol. 85: 106654. https://doi.org/10.1016/j.intimp.2020.106654.

Souza DC, de Faria LS, Sousa JEN, Lopes CA, Ribeiro VDS, da Silva VJ, Ribeiro RP, Rabelo ÉML, Rodrigues Ávila VM, Ferreira Júnior Á, et al. 2020. Use of polyclonal IgY antibodies to detect serum immune complexes in patients with active hookworm infection. Parasitology 147: 715–720. https://doi.org/10.1017/S0031182020000220.

Sudjarwo SA, Eraiko K, Sudjarwo GW, Koerniasari. 2017. The potency of chicken egg yolk immunoglobulin (IgY) specific as immunotherapy to *Mycobacterium tuberculosis* infection. J Adv Pharm Technol Res. 8: 91–96. https://doi.org/10.4103/japtr.JAPTR_167_16.

Sudjarwo SA, Indriyani W, Sudjarwo GW. 2014. Production and characterization protein of anti-HIV specific immunoglobulin Y for immunotherapy. J Appl Pharm Sci. 4: 30–34. https://doi.org/10.7324/japs.2014.4116.

Tabll AA, Shahein YE, Omran MM, Hussein NA, El-Shershaby A, Petrovic A, Glasnovic M, Smolic R, Smolic M. 2024. Monoclonal IgY antibodies: advancements and limitations for immunodiagnosis and immunotherapy applications. Ther Adv Vaccines Immunother. 12: 25151355241264520. https://doi.org/10.1177/25151355241264520.

Teimoori S, Arimatsu Y, Laha T, Kaewkes S, Sereerak P, Sripa M, Tangkawattana S, Brindley PJ, Sripa B. 2017. Chicken IgY-based coproantigen capture ELISA for diagnosis of human opisthorchiasis. Parasitol Int. 66: 443–447. https://doi.org/10.1016/j.parint.2015.10.011.

Thirumalai D, Rajesh R, Vignesh S, Chang CC, Feng CH. 2019. Chicken egg yolk antibody (IgY) as diagnostics and therapeutics in parasitic infections – a review. Int J Biol Macromol 136: 755–763. https://doi.org/10.1016/j.ijbiomac.2019.06.118.

Thomsen K, Christophersen LB, Bjarnsholt T, Jensen PO, Moser C, Hoiby N. 2015. Anti-*Pseudomonas aeruginosa* IgY antibodies induce specific bacterial aggregation and internalization in human polymorphonuclear neutrophils. Infect Immun. 83: 2686–2693. https://doi.org/10.1128/IAI.02970-14.

Thu HM, Myat TW, Win MM, Thant KZ, Rahman S, Umeda K, Nguyen SV, Icatlo FC Jr, Higo-Moriguchi K, Taniguchi K, et al. 2017. Chicken egg yolk antibodies (IgY) for prophylaxis and treatment of rotavirus diarrhea in human and animal neonates: a concise review. Korean J Food Sci Anim Resour. 37: 1–9. https://doi.org/10.5851/kosfa.2017.37.1.1.

Tong C, Geng F, He Z, Cai Z, Ma M. 2014. A simple method for isolating chicken egg yolk immunoglobulin using effective delipidation solution and ammonium sulfate. Poult Sci 94: 104–110. https://doi.org/10.3382/ps/peu005.

Wang F, Qiao W, Bao B, Wang S, Regenstein J, Shi Y, Wu W, Ma M. 2019. Effect of IgY on periodontitis and halitosis induced by *Fusobacterium nucleatum*. J Microbiol Biotechnol. 29: 311–320. https://doi.org/10.4014/jmb.1810.10044.

Wang X, Song L, Tan W, Zhao W. 2019. Clinical efficacy of oral immunoglobulin Y in infant rotavirus enteritis: systematic review and meta-analysis. Medicine (Baltimore) 98: e16100. https://doi.org/10.1097/MD.0000000000016100.

Wang Z, Ge S, Meng L, Gao F, Xie Y, Zhang X. 2020. Canine parvovirus is diagnosed and neutralized by chicken egg yolk IgY scFv expressed in CRFK cells. Viruses 12: 1417. https://doi.org/10.3390/v12121417.

Wang H, Zhong Q, Lin J. 2023. Egg yolk antibody for passive immunization: status, challenges, and prospects. J Agric Food Chem. 71: 5053–5061. https://doi.org/10.1021/acs.jafc.2c07094.

World Health Organization. 2018. Dengue vaccine: WHO position paper, 2018.

World Health Oganization. 2020a. Global Turbeculosis report.

World Health Organization. 2020b. World malaria report 2020.

World Health Organization. 2021. Ebola. https://www.who.int/health-topics/ebola (accessed: 18.08.2025).

Wu R, Yakhkeshi S, Zhang X. 2022. Scientometric analysis and perspective of IgY technology study. Poult Sci. 101: 101713. https://doi.org/10.1016/j.psj.2022.101713.

Xu Y, Selerio-Poely T, Ye X. 2018. Clinical and microbiological effects of egg yolk antibody against *Porphyromonas gingivalis* as an adjunct in the treatment of moderate to severe chronic periodontitis: a randomized placebo-controlled clinical trial. J Periodontal Implant Sci. 48: 47–59. https://doi.org/10.5051/jpis.2018.48.1.47.

Yakhkeshi S, Isah MB, Sadeghi-Abandansari H, Zhang X. 2025. Advances in IgY antibody dosage form design and delivery strategies: current status and future perspective. Int J Biol Macromol. 300: 140291. https://doi.org/10.1016/j.ijbiomac.2025.140291.

Yakhkeshi S, Wu R, Chelliappan B, Zhang X. 2022. Trends in industrialization and commercialization of IgY technology. Front Immunol. 13: 991931. https://doi.org/10.3389/fimmu.2022.991931.

Zhang L, Bai Y, Tao J, Yang S, Tu C, Liu L, Huang X, Li L, Qin Z. 2024. Effects of feeding chicken egg yolk antibodies on intestinal cell apoptosis, oxidative stress and microbial flora of tilapia (*Oreochromis niloticus*) infected with *Streptococcus agalactiae*. Fish Shellfish Immunol. 150: 109596. https://doi.org/10.1016/j.fsi.2024.109596.

Zhang X, Vieira-Pires RS, Xu L. 2021. Development of IgY technology: a historical perspective. In: IgY technology: production and application of egg yolk antibodies. Cham: Springer. 3–14. https://doi.org/10.1007/978-3-030-72688-1_1.

Zhang X, Wu R, Chelliappan B. 2023. Proteomic investigation and understanding on IgY purification and product development. Poult Sci. 102: 102843. https://doi.org/10.1016/j.psj.2023.102843.

Zhang Y, Wei Y, Li Y, Wang X, Liu Y, Tian D, Jia X, Gong R, Liu W, Yang L. 2021. IgY antibodies against Ebola virus possess post-exposure protection in a murine pseudovirus challenge model and excellent thermostability. PLoS Negl Trop Dis. 15: e0008403. https://doi.org/10.1371/journal.pntd.0008403.

Zhou X, Ma S. 2018. Anti-lipopolysaccharide egg yolk antibodies enhance the phagocytosis of mammalian phagocytes. Biol Open 7: bio032821. https://doi.org/10.1242/bio.032821.