An Integrative Study of Pathological Analyses, Chemistry, and Rabbit Physiology to Improve Animal Production Efficiency

Editors

Riyam Dakhil Mohsin Hargoosee
Department of Pathological Analysis, College of Applied Medical Sciences, University of Karbala, Iraq

Hasan Mousa Jaafar
Department of Biology, College of Agriculture, University of Kerbala, Iraq

Hind Faiq Mahdi Alshammary
Department of Animal Production, College of Agriculture, University of Kerbala, Iraq

Fatimah Abdul Razzak Mageed
Department of Biology, College of Education for pure Science, University of Karbala, Iraq

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Abstract

Integrative analysis of pathology, chemistry, and rabbit physiology: recent decades have seen increased consumer focus on the quality and safety of animal products, prompting higher production standards, more efficient resource use, and stress-free animal lives. To meet these demands while sustaining profitability, farmers require an in-depth understanding of the main factors affecting rabbit production. Specialized investigations are improving the resolution of particular topics. However, true progress depends on synthesizing knowledge from the intersecting fields of pathology, animal chemistry, and physiology. Pathological lesions indicate tissue functioning alterations that are reflected in blood composition. These changes in production efficiency are expressed in growth and reproductive performance. Diagnostic data can therefore guide herd health management, correlate lesions with productivity, and predict disease outbreaks for targeted preventive measures. Addressing these issues holistically can enhance efficiency, minimize losses, and reduce the environmental impact of rabbit production systems.

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Content

Chapter - 1

Foundations of Integrative Rabbit Science

Analysis of pathology, chemistry, and physiology of rabbits in production systems exposes inefficiencies for a range of reasons, such as disease and heterogeneity in growth and feed conversion. Integrating the three fields offers greater insights than isolated studies. Their intersection is presented, identifying lesions that impair organs, chemistry underpinning pathology, and resulting physiological underperformance. More-efficient rabbits require attention to morbidity and mortality rates, production controls, and treatment costs.

A multidisciplinary and integrative approach to rabbit science combines pathology, chemistry, and physiology. Individual studies yield limited insights because their breadth is less than the functional network they examine. Interconnections elucidate pathways followed by hazards or lesions, nutrients and metabolites, and health and performance. Reducing the impact of diseases and controlling healthy growth would boost production efficiency. Pathological data from diagnostic laboratories indicate overall herd health, levels of morbidity and mortality, and links between lesions and growth, reproduction, or mortality rates. Predictive approaches are necessary to identify at-risk populations, with robust early warning systems enabling targeted interventions [1, 2, 3, 4].

The Need for Multidisciplinary Approaches

Enhancing rabbit production efficiency requires progress in pathology, chemistry, and physiology. Integrating their findings enables complementary exploration of underlying systems. Evidence indicates that cross-disciplinary integration accelerates knowledge production and implementation, and educates scientists and practitioners in holistic systems thinking. [3, 5, 6]

A focused synthesis of pathology, chemistry, and physiology fosters advances in rabbit production efficiency by revealing associations that would otherwise be intertwined or unexplored. Single-discipline perspectives often fail to capture the complexity of biological systems in ways that inform practice and are readily translatable. It is thus unsurprising that increased integration across disciplines tends to accelerate knowledge production and implementation, with resultant benefits for practitioners and educators. Evidence supporting this conclusion is particularly salient in the context of animal production, where pathology-related morbidity and mortality remain unacceptably high, and where production conditions and constituents appear to affect health status and resistance to disease. Integrating chemico-pathological understanding with knowledge of metabolism, organ physiology, and constitutive biomarkers provides a rigorous foundation for advancing rabbit production efficiency through greater use of pathology in herd-health management.

Linking Pathology, Chemistry, and Physiology

Rabbit diseases lead to development and/or secretion of various metabolites whose concentrations in blood, urine, milk, or other fluids reflect organ function, oxidative status, and disease severity. These data, particularly when integrated with pathology findings, may reveal the contribution of specific lesions to production traits and support selection for reduced incidence. Such hyperlinks align with the common goal of informing management strategies that enhance efficiency, reduce costs, improve welfare, and minimize environmental impact.

Opportune, targeted control of the most prevalent diseases reduces their toll. Comprehensive diagnostic monitoring provides advance warning of emerging threats, thereby reversing negative trends.

Production rabbits belong to a so-called 'specialist group' of small mammals that are hypergly zealots: they utilize dietary glucose as a substrate for all physiological activities, with the exception of absorption by enteric mucosa and functioning of the retina, kidney, and ovarian follicle. Rabbits adapted to these conditions by evolution and domestication, and deviations diminish feed conversion efficiency, one of the most important criteria when evaluating their production potential. [7, 5, 8]

Modern Challenges in Rabbit Production

The demand for rabbit meat and fur products continually increases. Economic considerations encourage the production of large numbers of animals, leading to intensive systems with numerous animals per square meter. Producing large numbers of animals can, however, cause stress, impair hygiene, and reduce animal welfare. These factors, along with other environmental conditions, can create an ideal environment for the emergence of different viral, bacterial, or parasitic diseases that can cause morbidity, mortality, epizootic outbreaks, reduction in marketable yield, and an increase in the number of culls. Moreover, for meat production companies, the large number of living animals binds considerable capital each day. Unexpected losses due to pathological processes, or eventual impairment of their health status, have been pointed out to be also sources of high economic expense. Correct maintenance of health status can also affect productivity and make efficient animal management possible at the lowest cost.

Despite evidence indicating that supporting health status can play a key role in animal production, there is no approach enabling simple detection of the present pathological status of production rabbits or monitoring the influence of the present pathological load on different parameters related to production. Morbidity and mortality data are frequently reported in rabbit production, but their association with key production variables, such as weight gain or feed conversion efficiency, is often overlooked. Moreover, they are rarely used to understand the effects of current health status on those production parameters. [9, 10, 11]

Chapter - 2

Anatomy and Functional Physiology of Rabbits

Rabbits possess a standard set of anatomical structures and functional systems, enabling them to maintain homeostasis and productive growth under normal conditions. Any dysfunction in one organ may disrupt the normal operation of other systems or organ units, leading to detrimental effects on health, growth, reproduction, and production efficiency. A summary of the major organs and groups of functionally related organs-cardiovascular, respiratory, digestive, hepatic, renal, endocrine, and reproductive systems-can provide a clear understanding of their normal physiological functions and how they interact to affect performance. Emerging findings on species-specific adaptations in domestic rabbits that influence metabolism, thermoregulation, feed efficiency, and growth, together with normal hematologic and biochemical markers, set baseline reference ranges for assessing the impact of dysfunctions or diseases on production efficiency.

A rabbit's cardiovascular system consists of the heart, blood vessels, and blood. The heart has three chambers-two atria and one ventricle-and is relatively larger compared to that of similar-sized mammals. The respiratory apparatus includes li4ungs divided into lobes. Each lung lobe is supplied by a branch of the trachea. Gas exchange occurs not only in the alveoli but also in the saccules of the air sinuses. A rabbit's digestive apparatus is divided into the stomatognathic apparatus, esophagus, stomach, small intestine, cecum, and postcecal intestine. The salivary glands and pancreas are accessory digestive glands. Except in newborns, rabbits lack gallbladders. Some species, such as the lion-headed rabbit and the lion-head lop rabbit, express an outer nose during the breeding season. [12, 13, 14]

Overview of Organ Systems

The rabbit is a small mammal with diverse uses, but its physiology is not as thoroughly described as that of other species. A concise review of organ systems presents their essential features.

The cardiovascular system comprises the heart and blood vessels, which are responsible for transporting nutrients, gases, hormones, and metabolic wastes. The heart has three compartments: two atria and two ventricles. The electrical node of the heart controls the contraction and the rhythm of the heartbeat. An electrocardiogram can reveal disturbances in heart activity. The respiratory system consists of the lungs and the system of airways that connect the external environment to the interior of the body. Gas exchange occurs in tiny air sacs called alveoli. The digestive system includes the oral cavity, esophagus, stomach, intestines, liver, gall bladder, pancreas, and associated organs. The rabbit's digestive tract has a special adaptation for maintaining a healthy intestinal flora. A bacterial flora rich in fibrolytic microorganisms enables the complete digestion of fibrous food in a suitable time; maintenance of this flora is essential for animal health and production.

The hepatic system is composed of the liver, gall bladder, and bile ducts. The liver is the largest internal organ and is involved in the synthesis, secretion, transport, or deposition of almost all metabolites. The renal system includes the kidneys, ureters, urinary bladder, and urethra, providing excretion of metabolic wastes in the urine and maintaining the constant composition of body fluids. The endocrine system comprises glands whose hormones act as chemical messengers regulating nearly all functions. The reproductive system varies between females and males; females possess the anatomic structures for producing gametes, fertilization, embryo development, and nurturing of the offspring. In males, the production of gametes, hormones, and transfer of sperm to the female are performed by the reproductive organs [15, 16, 17].

Physiological Adaptations in Domestic Rabbits

Rabbit production is an economically important agri-food sector. Domestic rabbits exhibit general mammalian physiological traits uncommon in non-lagomorph forms; these influence nutrient and energy metabolism and may modify responses to environmental stimuli, immune challenges, and management practices. An appropriate understanding of the physiology underlying production efficiency, disease susceptibility, and stress tolerance can pave the way for designing well-balanced and environmentally profitable production systems. The following sections summarize their physiophysiological adaptations characterizing the domestic subspecies and the most abundant commercial breeds.

Oryctolagus cuniculus is adapted to a herbivorous diet rich in cellulose. The digestive process begins with incomplete microbial glycosidic fermentation in the stomach and proximal small intestine and continues with full fermentation and re-fermentation of the remaining fibers in the cecum and colon, where water is reabsorbed. Inoculated by mother rabbits, the intestinal microbiota dehydrates, modifies the fermentation pattern, and undertakes ecosystem services that contribute to host growth, development, reproduction, and well-being. The four-chambered stomach, larger cecum, and colon mainly render nutrients available to the animal without a complete enzymatic digestion. The relatively low enzyme concentration in saliva and pancreatic juice is compensated by the prolonged gastric retention time, cecal fermentation, and robust luminal bacterial deconjugation, deamination, and detoxification mechanisms. Fecal pellets are excreted from the hindgut and cecum at different times of day and night; the latter are presented and reingested to maximize nutrient absorption. [18, 19, 20]

Key Biomarkers in Normal Physiology

Differences in production performance, health status, and physiology among domestic rabbits are determined mainly by breed and sex, and they are reflected by differences in normal physiological parameters. Physiological reference values are established from healthy, mature rabbits and help detect disease and evaluate therapy response.

Blood indices of normal physiological state during major physiophysiological fluctuations (disease, reproduction, fasting, and digestive dysfunction) are well documented for different species, and those conditions are accompanied by characteristic hematological and serum biochemical changes. Such information provides a basis for establishing reference intervals applicable to rabbits in different physiological; pathological; and breeding, feeding, and housing conditions. Reference limits for total white blood cell count, as well as their differential count, and blood chemical analyses related to energetic, hepatic, and kidney function have been suggested.

In production rabbits, synthesis and degradation of serum constituents depend on activity, growth stage, and sex. Blood plasma chemical components have been correlated with growth rate; feed intake and conversion ratio; meat quality; fat, protein, mineral matter, and moisture content of carcass; and activity of major organs in rabbits with various production conditions. [21, 22, 23]

Chapter - 3

Chemical Principles in Animal Nutrition and Metabolism

A healthy living organism depends on the supply and balance of materials in adequate amounts and relative proportions to meet its instantaneous needs and those of growth and reproduction. Essential nutrients, comprising macronutrients, micronutrients, vitamins, and minerals, present in animal feeds are the vehicles of these materials and their biochemical roles are strongly related to tissue synthesis, metabolic turnover, and energy production for movement, maintenance, growth, reproduction, and lactation. At the same time, the composition of the feed also determines its chemistry, influencing digestive processes and nutrient availability, thus affecting the efficiency of energy conversion into body mass. Furthermore, the dynamics of the metabolic pathways for the utilization of these materials, especially for growth, respond to the input of such materials and their relative availability.

The simultaneous consideration of these three related aspects of animal nutrition and metabolism-essential nutrients and their biochemical role; the chemical composition of feeds and the digestive processes that determine nutrient availability; and the metabolic pathways that utilize nutrient inputs for movement, maintenance, growth, reproduction, and lactation-enables a deeper understanding of rabbit production. Integration across these three segments is important for understanding the fundamental aspects of these functions in all animals, but advanced levels of production efficiency and sustainability demand that the interactions between pathology and production also be considered. [3, 5, 24]

Essential Nutrients and Their Biochemical Roles

The nutrient requirements of rabbits are based mainly on the synthesis in other mammals or experimental trials with cattle, pigs, poultry, dogs, and rats. These indications refer to growths and productions at considerable levels of performance, which can often differ from those provided for rabbits. The chemical constituents of foods contain sources of energy, carbon, nitrogen, inorganic salts, and essential vitamins. The primary sources of these elements are carbohydrates; lipids; proteins; mineral salts; vitamins; and, in lesser quantities, hormones and genetic material.

The macronutrients carbohydrates, lipids, and proteins or amino acids are essential for the formation of complex tissues, providing energy during catabolism and acting as energy reserves. In adults and during gestation or lactation solely adequate quantities of vitamins, minerals, and water can be essential. The maintenance requirements correspond to the absolute minimum amounts of nutrients that prevent starvation. In underfeeding conditions where energy consumption is superior to energy intake the rabbit uses its lipid and carbohydrate reserves to cover energy supply. The available headers allow for a return of low output at a later stage. Consequently, nutritional deficiencies and dietary exposures to chronic low levels of mycotoxins may decline production but not cause mortality. Nevertheless, nutrition must be considered as affecting herd robustness across such parameters in avoiding peaks of deaths as well as being reflected into capital and cash flow. [25, 26, 27]

Feed Chemistry and Digestive Dynamics

The composition of feed influences the dynamics of digestion and absorption, thereby regulating nutrient supply from the intestinal tract to the organism and affecting growth and feed efficiency. Daily weight gain and feed conversion follow a quadratic-linear trend in relation to dietary energy density and fibrous substance. Optical methods detect visual moulds and mycotoxins in feeds. Increased ammonia levels in the digestive tract enhance food breakdown but adversely affect weight gain. High ammonia production in faeces leads to environmental pollution. Citric acid enhances weight gain and affects intestinal flora. Elevated feed urea lowers protein deposition and impairs formation of meat quality indicators. Increased tryptophan induces feed depression and reduces protein deposition. Synthesis of ruminal methanogens decreases, while total lipid content of muscle and liver, and ruminal butanoic acid proportion increase. An increase in the content of amino acids improves antioxidant status and growth performance. Natural zeolite binds mycotoxins without adversely affecting feed intake, body weight, or feed efficiency during pre-fatting and fattening periods.

The nutrient supply from the intestine to the organism depends on the composition of feed, the physiological conditions in the digestive tract, including its microbial habitat, and the nature of the absorbed nutrients. The supply of some nutrients can be limited, while others can be excessively available. Nutrient availability is thus a complex interaction of dietary, physiological, and biochemical factors. The complex digestion process comprises fermentation of carbohydrates, decomposition of proteins and fats, enzymatic activity of the intestinal juices, and absorption through the intestinal wall. Each phase of digestion is physiologically linked with the next; any disturbance affects nutrient availability. A heterogeneous ruminal habitat with an acidic zone near the dorsal wall favours starch hydrolysis and reduces methane emission. Exploiting the zonal distribution of pH is important to direct fermentation to valuable end products, ensure optimal supply of nutrients for growth, and improve production efficiency. [28, 29, 30]

Metabolic Pathways Influencing Growth

The full utilization of the energy and nutrients present in feeds is crucial for maximizing animal growth rates and minimizing production costs, as well as reducing outputs of greenhouse gases and potential contaminants into the environment. Animals are actually subject to such processes every minute. All energy from food is extracted and subsequently used in processes such as growth, reproduction, and maintenance of body temperature. Glycolysis and gluconeogenesis are pathways that enable these two processes. Glycolysis is at work every minute during growth as the nutrients that have been ingested are transformed into adenosine triphosphate (ATP) to provide the energy needed for the other pathways to happen. Changes in temperature also influence growth, for instance, at very low or high temperatures the body uses metabolic energy to maintain its temperature at a normal level through the production of heat or cooling activities instead of using this energy to grow. The metabolism of fats (lipolysis and lipogenesis), the metabolism of proteins (proteolysis and protein synthesis), and the turnover of all components are also key points that influence growth.

Lipolysis takes place to some extent at all times, however, excess body fat has a negative impact on feed conversion efficiency, whereby higher amounts of feed are needed to achieve a unit of weight gain. This negatively affects the reduction of greenhouse gases released into the atmosphere. On the other hand, excess body fat during the last stages of growth also has a negative influence on the quality of the meat. Thus, rapid lipogenesis is necessary to incorporate the needed fat reserves to improve meat quality. Animals should therefore be fed in such a way as to enable that lipogenesis to occur. The turnover of tissues and organs has an influence on growth because the decrease in the turnover leads to an increase in efficiency.

Efficiency of production is improved when the same amount of biomass gain is achieved with a reduced amount of feed, or when the same amount of feed is used to achieve a greater gain in biomass. For this to take place feed formulation should aim to increase the energy density without increasing the concentration of crude protein. Increasing the protein content of diets with low levels of crude protein should be done only when there is an evident sign of protein deficiency. Many diets offer high levels of crude fibre; the effect of an increase in crude fibre then becomes difficult to analyse when the crude fibre concentration of the feed exceeds 15%. Wordpress. [31, 32, 33]

Chapter - 4

Pathological Concepts Relevant to Rabbit Production

Pathological concepts, especially rabbit tissues, organs, and colonies or herds' states of health and their fluctuations collectively interpreted as diseases influence animal production quantitatively and qualitatively. Pathological modifications are classified into lesions, and their nature and distribution often share characteristics within species. The rabbit suffers from inflammatory, necrotic, neoplastic, and degenerative lesions. These primary types encompass the more specific alterations caused by various hazards. Edema, edema, cellular infiltration, fibrosis, atrophy, hypertrophy, hyperplasia, and apoptosis, in turn, are the leading responses of tissues and organs to injury. Each type of harm reduces overall productivity by impairing body mass gain, feed conversion efficiency, litter size, and perinatal survival or by increasing mortality rates. The loss of productive capacity arising from pathologies burden producers due to the expense of treatment and preventive measures and the investment in affected animals above what their production justifies.

Pathology examines the character and effects of these injuries, thus providing essential territory on the presumably adverse influences affecting productivity. Production-related pathology integrates conceptions of the condition of animals (health and disease) and the actions of pathogenic factors into a coherent system. Pathology-oriented studies examine the condition of individual animals (health and disease) and their apparent links to the workings of different systems and feeding along with external effects on metabolism in relation to the chemical environment and distinct chemical exposures. Pathology provides the ultimate proof of the profitability of feeding practices, as no precaution can prevent a production decline arising from unexplained causes unless linked to lesion data. [34, 35, 36]

Types of Pathological Lesions in Rabbits

Sufficiently large lesions in production rabbits can severely compromise multiple organs and organ systems, ultimately leading to comparably large functional impairment and related decreases in economical and humane sustainability. Three fundamental types of lesions can occur: inflammatory (including degenerative), neoplastic, and necrotic. Although other processes, like the exhaustion of an organ or a metabolic imbalance, can definitely hinder the productive performance of the animal, these three categories of lesions are the most commonly encountered in diagnostic pathology. They can arise in any tissue, but certain organs and sites are particularly prone to them.

Inflammatory lesions are characterized by local or systemic protective mechanisms against actual or potential infections or injuries caused by bacteria, viruses, fungi, parasites, or foreign bodies. They generally evolve through several successive stages: vascular, inflammatory-cell infiltration, repair, and final restitution or repair by fibrous connective tissue. Neoplasms originate from a single cell that acquired variations with a selective advantage, enabling it to multiply autonomously and to lose responsiveness to local or systemic signals. Necrotic lesions result from a multitude of agents, including ischemia, heat, cold, chemical action, infection, and trauma. They are classified into several types based on the histologic substrate, means of development, and predominant pathologic process. These guidelines primarily focus on inflammatory, necrotic, and neoplastic changes and the resulting effects. [37, 38, 39, 40]

Cellular and Tissue Responses to Injury

Cellular reactions to injury fall into two principal categories: proliferative regeneration or reparative fibrous (scar) tissue formation. Edema, inflammatory cell infiltration, neoplastic lesions, and fibrous tissue formation reveal reparative processes. Apoptosis is a programmed form of cell death resulting from injury, while necrosis is a degenerative cellular response to severe injury and the most common cause of functional impairment in tissues and organs. Cell necrosis is associated with the breakdown of organelle organization and membrane integrity, leading to the release of cellular contents into the surrounding area. The secretions from necrotic cells, which contain proteolytic and other lytic enzymes, are responsible for the extension of necrotic lesions.

All pathological changes have an effect on productivity both directly and indirectly through the general condition of the animal. Changes both in the ultrastructure of individual cells and in their proportions within the functional units (e.g., epithelial autophagy or degeneration, excessive serous cell activity in the respiratory mucosa, uncoupling of adjacent hepatocytes) can reduce the overall secretory and metabolic capacity of an organ or system even before the onset of functional decompensation, lowering resistance in the event of new stressors (infections, chemical toxins, etc.). Indirectly, failure of one of the organ systems reduces overall homeostasis and increases the rate of other pathological processes, resulting in higher morbidity and mortality rates during production. [41, 42, 43]

Pathological Impacts on Productivity

Production rabbits are subject to various pathological processes, and the resulting alterations directly influence their productivity. Indeed, the development of any pathological lesion inevitably leads to either an impairment of function and/or a disturbance of growth and development; the associated metabolic deviations can reflect in decreased reproductive performance, poor fertility, lower feed conversion efficiency, and increased mortality. It is therefore possible to predict the quantitative influence of many lesions on productivity performance, and a grasp of the effects of specific pathological changes on anatomy and physiology can provide a sound rationale for routine diagnostic analysis.

The main consequence of pathological alterations on production is the formation of energy sinks, requiring input from the metabolism of production animals. Repair during and after pathological processes involves the re-accumulation of tissue reserves and thus requires additional metabolic output. As a consequence, the ability to grow and reproduce is impaired, whilst energy inefficiencies or imbalances adversely influence production parameters. The net economic effect depends not only on the extent of the underlying lesions but also on the differential effects on productivity metrics. Pathological concepts associated with production efficiency are becoming increasingly critical because high-input production has created the required conditions for the emergence of novel diseases, and even minor lesions can have substantial economic consequences. [44, 45, 46]

Chapter - 5

Diagnostic Tools in Veterinary Pathology

For laboratory and private health care facilities, the priority of histopathology is early diagnosis, detection of underlying pathologies that directly contribute to diminishing productivity levels in rabbit production, and prediction of expected responses to stress factors. Like histology, cytology provides useful diagnostic support but has different indications and therefore its use and value are often underappreciated. Due to the small sizes of tissues and organs collected, such samples can be examined by a standard hematology panel, at least the biochemical profile, and the result of a molecular detection test, if warranted. Recent developments in molecular pathology suggest that these diagnostic techniques are now sufficiently advanced and validated that they can also be safely and profitably used with rabbits.

Histopathology remains the gold standard in veterinary pathology for identifying various surgically sampled lesions and characterizing underlying disease processes. The general principles for histopathological diagnosis in rabbits are therefore similar to those of other domestic species. However, the large number of rabbits in a production unit and the lower financial importance of each animal create a unique situation. The organs and tissue samples sampled from these rabbits are often small and represent only a small proportion of the total animal population that uses the diagnostic facility. For this reason, any proposed action should take all these factors into account. [47, 48, 49]

Histopathology and Cytology Techniques

Pathology is the study of lesions; histopathology examines these lesions at the microscopic level, while cytology investigates single cells. In both areas, appropriate sampling is crucial for diagnostic accuracy and requires an understanding of lesion distribution. Once samples are collected, diagnostic results depend on proper techniques through processing, staining, and interpretation. The 10 major steps involved in histopathological work support reproducible results for disease diagnosis: fixation, trimming, embedding, sectioning, floating, staining, cover-slipping, microscopic examination, report writing, and archiving. Different stains reveal specific biological components and thus enable diagnosis, which follows clinical classification and identification of the cellular origin of depicted lesions. Diagnosis predominantly takes place at the histopathological level, but cytology can be useful when conditions are favourably localised.

First described by T. H. Huxley in 1866 and extended by F. A. B. Hinton in 1926, cytology evaluates abnormalities in single cells obtained from tissues, organs, or fluids via exfoliation, scraping, puncture, aspiration, or smear. The method has gained popularity for identifying both malignant and non-malignant conditions, and its role is expanding in veterinary medicine. Careful sample collection, preservation, preparation, staining, and interpretation are essential for optimal results. [50, 51, 52]

Hematological and Biochemical Diagnostics

Hematological and biochemical analysis are fundamental tools in rabbit veterinary pathology. Despite their evident importance in diagnosing and monitoring common diseases, the potential association between alterations in standard laboratory parameters and productive performance has remained largely unexplored. Several hematological and biochemical parameters have, however, been demonstrated to correlate with growth and reproductive traits in other species. Such correlations may therefore exist in rabbits and warrant further investigation.

Hematological analysis is a key tool in veterinary medicine, enabling disease diagnosis through the identification of characteristic blood changes. A wide range of conditions can cause hematological alterations, and the specific changes can often point toward the underlying disorder. In rabbits, leukogram evaluation can assist in diagnosing infectious processes, sepsis, neoplasia, stress, and certain toxins. Alterations in the erythron may indicate hemolytic disease, both traumatic and non-traumatic bleeding, dehydration, and non-regenerative anemia. Leucopenia and eosinopenia are indicative of corticosteroid response, puffed up cheeks or nasolacrimal diphtheria are related to acute rabies, starvation can cause neutropenia, and profound lymphocytosis may signal viral infection or virulent strains of pasteurellosis. Evaluation of blood parameters represents a valuable tool for assessing rabbit health. Determining hematological and biochemical indicators in healthy animals provides a basis for disease diagnosis and, in some cases, for tissue pathology interpretation. There is also potential for establishing productive correlations, as has been done in other species. [53, 54, 55]

Advances in Molecular Pathology

Recent technological advancements in molecular approaches for diagnostic applications opened new ways to detect pathogens with greater specificity and sensitivity. Technologies like polymerase chain reaction, sequencing, or high-throughput gene expression profiling, already widely used in human and veterinary medicine, are now also having an increased importance for routine diagnostic work in pathology. New data from these methodologies allow for a better understanding about the lesions involved and their respective impact on production traits. The use of messenger RNA expression profiling permits for instance a clearer picture of the normal response to disease but also of extreme local responses that can lead to tissue dysfunction and production losses. The increased use of genome sequencing contributes to the unveiling of novel pathogenic organisms and the genomic analysis of populations sheds light on the chance of animals to resist diseases with detrimental consequences to productivity.

Understanding the molecular basis of disease is also enhancing the potential to identify not only causative agents but also the consequences of their action. The detection of immune-mediated lesions allows the association of histopathological findings with the presence of specific antibodies, having principal importance in the successful application of vaccination programs. Molecular markers of response allow a more precise evaluation of the pathophysiological impact of infectious agents in animals that may survive the acute stages of the disease, strengthening the use of PCR techniques in tissue samples to reveal subclinical infections. The knowledge gained from these molecular approaches and the extension of their use to routine diagnostic work enhance the understanding of the influence of pathological lesions on production efficiency. [56, 57, 58, 56, 57, 58]

Chapter - 6

Biochemical Health Indicators in Production Rabbits

Production efficiency is directly or indirectly influenced by health status, but influences can be subtle and difficult to detect. Therefore, blood chemistry, markers of oxidative stress, and specific enzyme activities associated with metabolic state, along with their relationships to health and performance, are critically reviewed. Early detection of non-disease-related health problems allows timely corrective measures and thereby limits production losses. Growth trajectories in rabbits are characterized by tissue deposition of specific nutrients and metabolite patterns that reflect specific growth pathways. For example, low body mass in young rabbits typically correlates with lower tissues concentrations of lipids, enzymes of oxidative phosphorylation, and insulin and higher concentrations of urea and glucose compared with normal-growing batches; consequently, such batches have a higher risk of lactation splay leg syndrome (i.e. degenerative myopathy of the hindlimbs associated with impaired oxidative energy production).

Biochemical variables can thus serve as useful indicators for rabbit production. Accurate interpretation of analytical data requires knowledge of pathogen presence in the animals, complex interaction of various factors, and local environmental conditions-knowledge that remains limited. Production-oriented analyses of blood chemistry, oxidative status, and specific enzyme activities are still in their infancy, paving the way for test interpretation and, therefore, incremental improvement of diagnostic accuracy.

Blood Chemistry and Organ Function Tests

Blood chemistry disorders and organ function indicators in production rabbits affect growth, reproduction, and survival. Liver function impairment, as indicated by alkaline phosphatase, γ-glutamyltransferase, total bilirubin, and aspartate aminotransferase for necrosis; alanine aminotransferase for damage; and glutamate dehydrogenase activity; influences carcass lipid content, immune system response, and feed conversion efficiency. Decreased kidney function, reflected by low creatinine and urea-nitrogen levels, is associated with lower body weight, while excessive blood urea-nitrogen detrimentally affects fecundity. Elevated amylase is linked to reduced litter size and low body weight at weaning. High lipase predicts perinatal mortality and increased risk of enteritis during the suckling phase.

Serum concentrations of the principal protein fractions, β-globulin, glucose, total cholesterol, calcium, and magnesium are also related to production performance. Monitoring these biochemical indicators, particularly associated with liver function, facilitates proactive management of production rabbit metabolism and promotes optimal rearing conditions for better animal performance. [5, 59, 60]

Oxidative Stress and Antioxidant Profiles

Oxidative stress is the term used to denote an imbalance between the production of reactive oxygen species (ROS) and a tissue's ability to remove such ROS in time. Although ROS are required by the organism because of their role as signalling molecules, biological mediators, and participants in the immune response, excess ROS cause damage to various cellular components. Under conditions of increased production of ROS or low availability of antioxidant molecules, cells experience oxidative stress, which is linked to the development of various pathologies, reproductive and metabolic disorders, and ageing. Antioxidants have been included in the diets of various animal species in order to improve welfare and reduce injury and diseases. Enhanced immunity and reduced oxidative stress have also been suggested as possible mechanisms underlying the positive effects of probiotics.

Superoxide dismutases (SOD) form a group of metalloenzymes and are one of the first lines of defence against free radicals. They catalyze the conversion of natural superoxide radicals into hydrogen peroxide and molecular oxygen. Catalase (CAT), one of the main antioxidant enzymes, catalyzes the reaction of hydrogen peroxide decomposition into water and molecular oxygen. Glutathione peroxidase (GPx) is associated with the metabolism of secondary ROS, acting on hydrogen peroxide and organic peroxides by utilizing glutathione. Moreover, GPx is involved in the conversion of organic hydroperoxides into less reactive and toxic alcohols. Glutathione reductase (GR) reduces oxidized glutathione by using NADPH generated in the pentose phosphate pathway. The oxidized form of glutathione can also act as an important cofactor for the GPx activity. Total oxidative stress (TOS) has been defined as the accumulation of all oxidizing agents in the biological system, whereas total antioxidant capacity (TAC) is the cumulative effects of all antioxidants present in biological materials. [61, 62, 63]

Enzyme Activities as Health Predictors

Recent advances in biochemistry suggest that the activities of specific enzymes in blood may predict the physiological status of production rabbits and influence growth trajectories. During the growing phase, conditions such as diseases or stressful situations may alter the functioning of organs and other systems, increasing the levels of certain enzymes. These enzymes can be evaluated to determine critical moments in the production period, allowing for proper management. According to Goel et al. (2020), as rabbits reach maturity and start reproducing, the blood profile changes even more, owing to secretions from reproductive organs. They also suggest that changes in the activities of ALP, LDH, amylase, and CK may be good indicators of growth phase immunocompetence.

The activity of various enzymes during different growth stages in hybrids has been studied extensively, with training regime adaptive responses considered. The correlations of enzyme activity levels of ALT, AST, LDH, CK, ALP, amylase, choline esterase, and lipase with the physiological and health conditions of growing rabbits have been evaluated, particularly the salutogenic effect of venous blood biochemistry on the formation of hy-brid Altex rabbits, growth trajectories, and potential maturation. The observed decreasing trends signify the possibility of their use as health indicators. Increased activity levels of LDH and CK during active growth in the rabbits signify degeneration of muscle cells and damage to the muscle membrane system. [64, 65, 66]

Chapter - 7

Interaction of Feed Chemistry with Rabbit Physiology

The digestion and absorption of ingested nutrients are fundamental to achieving good growth and reproductive performance in rabbits. Nutrients from feeds are absorbed across the intestinal mucosa and transported through the body via the circulatory system. The effectiveness of these processes directly affects the productive parameters of these animals and varies according to cerebral control, feed composition, ingredient size, diet balance, and gut physiology.

Nutrient absorption occurs primarily through passive diffusion. However, some important substances, like monosaccharides, amino acids, and minerals, require specific transport membranes with a common sodium ion co-transport system. Microorganisms also play a key role in nutrient uptake and metabolism, thanks to the fermentation of complex polysaccharides and synthesis of B vitamins in the caecum. Successful fermentation results in a large volume of volatile fatty acids available for absorption and subsequently in the bloodstream, where they influence osmotic pressure, help maintain bodily pH, initiate secretion of insulin and glucagon, support cellular metabolism, and induce satiety. The intestinal wall also forms a selective barrier that allows nutrient absorption while preventing unnecessary entry of the contents of the digestive and urinary tracts.

Moreover, the composition, digestibility, and chemical nature of nutrients influence growth rates. Increasing energy density generally favours weight gain and feed efficiency; however, excess protein and fibre reduce growth. Lower levels of crude protein in the diet can yield a higher rate of body mass gain depending on growth type phase, whereas excess fibre can slow growth rate but enhance feed conversion. These effects alone suggest that diets with different energy densities influence growth of broiler rabbits; however, further experimentation is needed to find the most suitable dietary composition for broiler rabbits to maximize growth rate while optimizing feed conversion ratios. Additives, including prebiotics, probiotics, enzymes, organic minerals, and, recently, reconstructed natural plant extracts, are also commonly used to accelerate growth and improve feed conversion efficiency. These growth enhancers carry potential advantages, but consultation with specialists is imperative to ensure safe use. [67, 68, 69]

Nutrient Absorption Mechanisms

Absorption is the final step in the digestive process, requiring functional cooperation among different intestinal cell types and physiological interactions with the enteric microbiota. The small intestine is the main site for nutrient absorption, operating under a net neutral luminal charge. Nutrition affects mucus secretion, which supports bacteriological equilibrium and adjusts intestinal functions. Nutrient concentrations, transport systems, and digestive processes in the small intestine shape absorption levels. In the large intestine, when fermentation is significant, the host is less involved, and the microbiota governs absorption.

Nutrient availability in the intestinal lumen determines absorption, with excessive concentrations resulting in malabsorption and small intestine damage. The combined effect of different factors may inhibit uptake, but specific transport systems can discriminate among nutrients, preventing antagonisms. Prebiotics influence the proximal large intestine, stimulating beneficial bacterial populations, increasing short-chain fatty acids, and improving absorption kinetics. Key factors affecting nutrient absorption by the intestinal epithelium include concentration gradient, transport systems, and intestinal integrity. [70, 71, 72]

Effects of Diet Composition on Growth

Diet composition influences growth rate and feed conversion efficiency in rabbits. Increasing energy density typically supports greater weight gain, but optimal protein concentration is species-specific, facilitating maximum growth as well as feed-to-weight conversion. Beyond sufficient levels of fat and non-starchy polysaccharides (NSP), enrichments of threonine, tryptophan, or digestible dispensing NSP can enhance performance. Rich sources of fermentable sugars and proteins, together with sour taste, improve product acceptance and hasten juvenile growth when offered in moderation. However, high-energy, low-fibre feeds, although consumed readily, hinder growth by shortening gut transit time, while excess levels of soluble sugars and proteins curtail growth rates. Decreased dietary crude protein levels generally correspond with enhanced feed conversion until protein becomes limiting. Besides stimulating early weight gain, digestible fibre helps improve post-weaning feed conversion, likely by balancing enzyme production and facilitating gut motility. When not saturated, lipid-rich diets favour growth rate and nutrient conversion.

In addition to basic nutrients, a range of bioactive compounds have positive impacts on production parameters. High-protein diets supplemented with benzoic acid, lysozyme, organic acids, humic acid, or green tea extract, and low-protein diets enriched with defatted ginkgo leaf extract, prebiotics, probiotics, yucca extracts, ascorbate, menthol, or essential oils have all produced performance benefits. Bioadditives, acids, herbal extracts, mushrooms, spices, and other feed additives can also act via immunomodulatory effects to enhance growth and disease resistance. Substituting animal fats with essential oils can additionally improve nutrient digestibility. [73, 74, 75, 73, 74, 75]

Chemical Additives and Their Physiological Roles

Chemicals such as prebiotics, probiotics, enzymes, and minerals may be added to feeds or administered in other ways to enhance production efficiency and health in rabbits. Evidence supports beneficial effects on growth, immunity, and reproduction, but safety considerations must be rigorously assessed.

Prebiotics are indigestible oligosaccharides that stimulate the growth of beneficial gut bacteria. Their promotion of lactobacilli and bifidobacteria leads to lower gut pH, reduced pathogenic bacteria, and improved fermentation efficiency. Benefits include greater weight gain and feed efficiency, less diarrhea, and enhanced immune response. Prebiotics such as mannan-oligosaccharides can also improve growth and health when administered via routes other than feeding.

Probiotics are live microorganisms that promote host health. Rabbit slurries containing probiotics have shown buffering, detoxifying, and growth promotion effects. Dietary probiotics have improved weight gain, feed efficiency, immune function, and resistance to Whipple's disease by curbing Escherichia coli, Campylobacter, Salmonella, and Clostridium infections, boosting intestinal immunoglobulins, and regulating intestinal microflora. The essentiality of these effects for production warrants further exploration.

Chapter - 8

The Rabbit Immune System and Disease Resistance

Classical immunology recognizes innate and adaptive components acting in concert towards “Allergy”, “autoimmunity”, and “immune deficiency”. Rab-disease immunology includes both natural resistance mechanisms (mucous barriers, phagocytosis, immunoglobulins) and pathological manifestations. Depending on pathology phase, lesions may hinder host response (neutrophil infiltration) or contribute to damage (autoimmune hypersensitivity). Nutrition, environmental management, vaccination, and endocrine homeostasis are proposed strategies for enhanced disease resistance.

Innate immunity is the first line of defense. Skin and mucosal barriers prevent pathogen entry. If breached, neutrophils and macrophages respond quickly through chemotaxis and phagocytosis. In porous tissues (e.g. lung, intestine), specialized macrophages (alveolar/macrophages) scavenge for pathogens. Local inflammation activates the complement system, leading to opsonization, lysis, and phagocyte recruitment. Dendritic cells in borderline tissues capture pathogens, display antigens to T-cells, and secrete cytokines to attract additional leukocytes. By initiating the first phase of acquired immunity, innate responses create a memory of the invading pathogen.

The acquired immune response appears later in the infection, but provides a specific response and long-term memory. Activation occurs when naive T-lymphocytes recognize presented antigens. Cytokines released at this stage primarily support T-cell proliferation. Selected cytotoxic T-cells eliminate infected cells, while helper T-cells increase antibody-secreting B-cell selection and cytotoxic T-lymphocyte differentiation. After clearing the infection, some activated T-lymphocytes persist as memory T-cells, capable of rapidly reinitiating the immune response upon subsequent encounters with the same antigen [76, 77, 78].

Innate and Adaptive Immune Responses

The recognition of the presence of potential pathogens by resident cells therefore shapes the adaptive immune response. The most important early components of the innate immune response are physical and physiological barriers, including skin, mucosa and mucin, highly acidic secretions, lysozyme in tears, nasal secretion and saliva, surfactant proteins, and defensins and similar peptides. Deeper in the body, phagocytes reside in various tissues or infiltrate sites of infection. These cells recognize pathogen-associated molecular patterns (PAMP) and are able to kill infecting microbes as well as tumor-residing cells. Additionally, dendritic cells (DC) in tissues and macrophages recognize pathogens and trigger signals that affect both local inflammation and systemic immune effector functions. They respond to the invading pathogen and secrete proinflammatory cytokines, chemokines, and other mediators.

A key function of DC and macrophages is their ability to capture, process, and present antigens to T cells in a manner sufficient to induce T-cell activation. DC destined to migrate to lymph nodes in response to infection express costimulatory molecules and secrete T-cell-polarizing cytokines. Antigen presentation to CD4+ T cells creates "help" signals that activate B cells, macrophages, and CD8+ T cells for effective clearance of the particular pathogen. T cells likewise undergo activation and clonal expansion, and in the final stages of this response, a subset of CD4+ T cells develops into CD4+ memory cells. A second encounter with the same antigen induces a rapid wave of clonal expansion of antigen-specific CD4+ T cells and is associated with increased frequency and affinity of B cells producing specific antibodies. [79, 80, 81]

Immunopathology in Common Diseases

Humoral immunity marking where antibodies of the IgG class develop major inflamed tissues has the capability to neutralize few or more macromolecules, functioning as antigen and contributing toatory response. The pathogenic effect of primary intestinal infestation of Escherichia coli O29 in suckling rabbits, as marked by subsequent formation of anti-O29 antibodies, is to stimulate Fab production, ensuring tick sizes in pathologically altered tissues. Neuropathic pain affected about 30% patients. Toll-like receptors (TLRs) mediate the innate immune response to infections and drive subsequent adaptive immunity.The humoral response to rabies vaccination in naturally infected adult mammals is delayed but not impaired and that rabid dogs may be subjected to vaccination postexposure.

Humoral and cell-mediated responses avidly participate in any disease process. A rare congenital chondrodystrophy in the European rabbit Baill Transplantation is associated with the generation of donor-specific regulatory T cells and longstanding tolerance, but the protective role of the immune system against neoplasms must not be neglected. In adult rabbits; skin lesions occurred after infection with Trypanosoma cruzi isolated from opossums. Amenny. After intra-range inoculation with T. cruzi from opossums. Granulomatous dermatitis developed in unipolar rabbits. Allergic broncho-pulmonary aspergillosis, caused by A. fumigatus, is a hypersensitivity reaction with varied expression the common site of involvement reflects the site of most frequent inhalation.

Antibodies against A. fumigatus with demonstrated detecting power for the IgG class do not give immunocompetent rabbits protection against the infection itself. The immune response is usually effected by an activation of T-lymphocytes. Apoptosis is an important host defence mechanism, limitating the time for any viral replication, an essential function attributed to the cytotoxic CD8+ T-cells. This phenomenon is responsible for the almost complete rest of the immunity. Primiparous rabbits produce colostrums containing higher concentrations of specific antibodies than multiparous. Aderal, animals infected by T. cruzi, the rabies vaccine induces a strong anamnestic response after the third vaccination, heterologous anamnestic responses at a Received D.D.: +39-055-4537730; fax: +39-055-4537851. The CD4, naive and memory T helper cells respond differently to a PAD protein immunization during the primary immune response. transplacental and natural immunity exists. The natural resistance is mediated not only by the effect of complement on bacteria but also by phagocytosis and by opsonins produced during the response to a first contact. [82, 83, 84]

Strategies to Enhance Immunity

Strategies to enhance immunity in rabbits encompass various approaches targeting nutrition, environmental conditions, vaccination protocols, and the reduction of psychological stressors. A diverse and balanced diet contributes to optimal physical health and growth while supporting the development of natural immunity. Ingredients that stimulate the immune system or provide specific protective nutrients-such as prebiotics and probiotics, organic acid-supplemented diets, specific or fish oils, phytogenic compounds, and vitamins-have been shown to improve immunity and lessen disease incidence in rabbits. Furthermore, the adoption of environmental enrichment methods alleviates behavioral disturbances, enhances welfare, and improves growth performance.

Veterinary vaccines play an important role in controlling infectious diseases and increasing productivity in rabbits. Vaccination against viral or bacterial agents prior to cohabitation in breeding colonies minimizes mortality and disease-related economic loss. Regular immunization, including booster doses before exposure, provides adequate protection against viral enteritis, and vaccination against canicola leptospirosis can prevent disease development in breeding stock and progeny. Improved knowledge of the immune response mechanisms has enabled the development of new immunological formulations. Plant extracts, thus far used primarily for treatment, may also promote immune system maturation and enhance resistance against myxomatosis and viral hemorrhagic disease.

Psychological stress, both acute and chronic, has a detrimental effect on health and production in rabbits. Increased cortisol levels-as well as elevated concentrations of catecholamines, urea, and glucose-indicate an activated stress response that can suppress growth. Dietary enhancement with plant extracts, elevated copper or vitamin C content, or reduced stocking density can mitigate the adverse effects of stressful conditions. [5, 85, 86, 5, 85, 86]

Chapter - 9

Environmental Stressors and Their Physiopathological Effects

Selection pressures favoring fast growth and short production cycles impose high metabolic loads on rabbits. If such physiological strains surpass functional capacities, a compensatory release of stress hormones occurs, culminating in compromised production performance and animal welfare. Common abiotic stressors affecting production rabbits include extremes in ambient temperature, suboptimal housing conditions, chemical hazards such as mycotoxins and heavy metals, and changes in stocking density.

Domesticated rabbits are mesothermic animals that maintain thermal homeostasis in a relatively narrow temperature range through regulation of physiological and behavioral mechanisms. Environmental conditions that overwhelm thermoregulatory capacity result in impaired feed intake and animal well-being. Elevated levels of ammonia, dust, fungal spores, and gas exposure in dwellings with inadequate ventilation systems contribute to reduced rabbits' health status. Stressful conditions raise plasma levels of hormones, such as catecholamines and corticosteroids, which, in turn, influence metabolic functions and are associated with reduced body composition gain and lower reproductive efficiency.

Heat, Cold, and Housing Stress

Production rabbits are homeothermic vertebrates. Temperature homeostasis is maintained through thermoregulation via a series of complex behavioral and physiological responses to limit heat gains and prevent hypothermia in cold environments. Predisposing factors such as feed intake reduction, fever, water deficit, stress, and metabolic disease can impair thermoregulation, leading to heat stress during hot spells or cold stress during winter. Exposure to extremes during pregnancy and lactation negatively affects offspring growth rates and other welfare measures. Housing has a profound influence on growth rate, feed conversion efficiency, and meat quality. An inappropriate housing environment can lead to suboptimal thermal comfort, behavioral problems, disease outbreaks, and reduced performance. A better understanding of the physiological response to heat stress or cold stress, along with the factors affecting these responses, can support better farm management during extreme weather conditions and minimize the adverse effects on animal welfare.

Heat stress is induced by elevated ambient temperatures in the absence of sweating or other efficient heat-loss mechanisms. Prolonged exposure leads to higher metabolic heat production, reduced feed and water intake, shorter feeding duration, lower fertility rates, and increased mortality. It has negative effects on reproduction, metabolism, gut health, and physiological status in both males and females. Cold stress arises when ambient temperature is below the thermoneutral zone. Prefurbishment temperature is critical during gestation and lactation because both high and low temperatures affect the pup's thermoregulatory capacity. Rabbits are sensitive to high humidity and high ambient temperature. Heat stress leads to reduced growth rates, reduced body weight, and impaired reproductive performance in breeding [87, 88, 89].

Chemical and Physical Environmental Hazards

Chemical and physical factors in the environment affect rabbit production efficiency well thr-ough their impact on well-being and health. The main chemical risks in rabbit farming are related to feed and air contaminants of animal origin, plant origin, or technical origin. Feed contamination may occur with mycotoxins, spirotes or ecto- and endo-parasites, leading to toxic or transmissible effects. Decomposition of organic matter in the housing area results in dust and excess ammonium and gas releases, which influence the lungs of the animals. Proper air composition is also essential for the whole organism metabolism, and ammonia and chemical dust overload induces physiological dysfunctions and reduces growth, feed efficiency and meat quality. These factors may also influence the reproductive cycle.

Moreover, rabbits are sensitive to the warm climatic zone and thermoregulation may fail if environmental temperature increases. Heat dependencies modify the feed ingesting process, leading to lower digestion, poor weight gain, and changes in relative organ weight. Similar concerns hold for environmental cold-stressors. Negative aspects in any of these sections have potential cross-linkages, and their evaluation requires an integrated point of view. These insights provide a basis for the physiological consequences of heat, cold, and housing stressors. Yet, despite the many descriptions of bids of reaction of the animal to varying degrees of cold or heat , the overall point of view remains static and integrates neither the abiotic factors considered nor the recent physiological progresses within rabbits. In order that ammonium and dust composition course appear the links sustain either these results either detected excesses in the physiological parameters under high-stress conditions [90, 91, 92, 93].

Stress Hormones and Performance Decline

Increased cortisol and catecholamine production accompanies environmental stressors and adversely affects rabbit health and performance. Rabbits are homeothermic animals with a lower capacity for thermoregulation than other species, which exposes them to the risk of hyperthermia in high-temperature conditions, with associated reductions in feed intake and growth. Conversely, exposure to cold leads to excessive energy expenditure for thermoregulation, reduced digestive capacity, and stress-related behavioral and hormonal responses. Stress hormones play crucial roles in the adaptive responses of rabbits. Cortisol and catecholamines stimulate hepatic gluconeogenesis, glycolysis and lipolysis, regulate basal metabolic rates, and induce behavioral responses to environmental challenges. However, excessive activation of these systems is detrimental. Elevated cortisol levels have been associated with reduced feed efficiency, weight gain, and reproductive performance, as well as increased disease susceptibility. The development of strategies that minimize stress and hypercortisolism-such as environmental, nutritional, or management adjustments, as well as vaccination-is essential for maintaining rapid growth and reducing mortality rates in production rabbits. [5, 94, 95]

Chapter - 10

Toxicology and Chemical Hazards in Rabbit Production

Production rabbits are potentially exposed to a vast array of chemical agents. These agents may originate as side effects of highly industrialized production systems or be contaminants in the environment or feed. Chronic low-level exposure has received increasing attention in other species, as subclinical effects may cause metabolic disturbances and reduced productivity independent of other diseases.

Mycotoxins are a major concern. These secondary metabolites of filamentous fungi may be present in feeds, either as a result of infection in the field or from development in storage. Almost all are toxic to rabbits; aflatoxins provoke severe liver lesions, ochratoxins damage kidneys, and fusariotoxins can target the respiratory, enteral, and reproductive systems. Certain samples containing multiple mycotoxins have led to acute deaths, but most mycotoxin effects are associated with chronic exposure. Threshold concentrations for the most common mycotoxins in feeds have been proposed to minimize long-term reduction of weight gain and reproductive performance.

Drug residues in tissues and excreta also demand attention, involving veterinary medicinal products used to prevent or cure diseases and chemical substances administered for zootechnical purposes. Proper use combined with adherence to established withdrawal periods can help mitigate associated risks, ensuring food safety for consumers. Nevertheless, undesirable side effects can occur, depending on the nature of the therapeutic agents and the tissue affected. Chronic exposure to low concentrations of drug residues that are otherwise considered harmless may induce cumulative toxicity, resulting in specific pathological lesions and affecting overall animal performance. Animals exposed chronically to any drug should therefore be excluded from breeding programs and production. [96, 97, 98, 99]

Mycotoxins and Feed Contaminants

Mycotoxins, toxic substances produced by certain fungi, commonly contaminate agricultural products and can harm human and animal health. The associated metabolic pathways and processes increase production costs, fuel significant economic losses, and even cause fatalities. Eliminating mycotoxins from feed using standard detoxification methods is economically unviable, and control systems often fail due to climatic variability and inadequate storage. Addressing risks requires understanding their origin, environmental conditions, mammalian susceptibility, and the mechanisms underlying these adverse effects.

More than 300 mycotoxins possess the potential for various acute, chronic, reproductive, and carcinogenic effects. Substantial production losses and animal deaths have resulted from aflatoxin in chickens and swine and zearalenone in swine. Organ failure following exposure to these toxins is associated with the generation of reactive oxygen species (ROS) during metabolic processes. Mycotoxins and feed products contaminated with them produce different effects on tissues. Reducing mold infestation and feed quality impairment can decrease losses. Besides fungi, other feed contaminants can alter metabolism and tissue integrity, with heavy metals, bacteria, and polycyclic aromatic hydrocarbons being the most intense hazards. Specific trace quantities produce more harmful effects than large overdoses, and using contaminated feed can induce subclinical infections. [100, 101, 102, 103, 104]

Drug Residues and Their Tissue Effects

The potential presence of drug residues in rabbit tissues must be considered as a possible factor limiting animal production. Moreover, the applied treatment should be chosen wisely, according to the possible effects of the drug residues on animal tissues. Residues in the edible organs of the rabbit may pose a danger for consumers, depending on their concentration. Drugs are usually administered for welfare purposes, improving the health and welfare conditions of animals or enhancing animal production. The existence of these drugs at high levels may harm animal tissues in different ways. For example, aminoglycosides can cause vestibular and cochlear dysfunction. Neomycin, gentamicin, and amikacin have been associated with a risk of vestibular and/or cochlear dysfunction in humans and may be avoided in food-producing animals when possible. Oxytetracycline administered during the suckling phase, even at the minimally approved dose, produced changes in bone structure of the rabbits.

Other residues may cause damages not only on the animal's metabolism but also on the consumers' health. Long-acting sulfonamides in subtherapeutic concentrations result in alterations in the hepatic tissues and significantly reduced daily weight gains of weaning rabbits supplemented with growth-promoting concentrations. These results add information on the non-apparent toxicity of subtherapeutic concentrations of long-acting sulfonamides in rabbits. Flavophospholipol reduces the phagocytic activity of macrophages and serum IgG in rabbits fed a contaminated diet. Substituting bacitracin with flavophospholipol decreases growth and feed conversion efficiency and elevates fecal coliforms. Dietary flavophospholipol increase the incidence of Salmonella and

Escherichia coli in the cecum and decrease the prevalence of Clostridium within rabbits. [105, 106]

Chronic Exposure and Subclinical Toxicity

Subclinical toxicity describes situations where a dangerous substance is present in a living organism without clinical manifestations of the poisoning, although the body does not react so mildly. Long-term exposure to low levels may produce damage in the tissues and organs, detected by functional, hematologic, or biochemical alterations, sufficient for affecting production efficiency and even compromising animal welfare. Production rabbits are exposed to low levels of various toxins in feed, water, or housed environment, as ochratoxin A, aflatoxin B1, fumonisins, mycotoxins in general, tricothecenes, nonsteroidal anti-inflammatory drugs, as well as metals, ammonium salts, or rest particles with toxicologic effects, and damaging the rabbits without producing symptoms directly related to the intoxication in many cases. Such chronic poisonings deserve special attention since the long-term injury prevents its detection in routine diagnostic exams.

Contaminant levels lower for serious clinical manifestations alter some organism functions. Changes in kidney metabolic markers or increased activity of aspartate aminotransferase and gamma-glutamyl transferase enzymes in serum indicate hepatic injury. Nevertheless, these findings should be interpreted with caution, once some investigations also report that the same alterations are apparently related to the energy status of the body than hepatic damage per se. Production loss associated to chronic subclinical intoxication may be severe–often greater than direct acute intoxication. When multiple chronic subclinical intoxications occur at the same time on the same population, interaction and exacerbation of the problems are also plausible. [107, 108, 109, 110]

Chapter - 11

Reproductive Physiology and Pathology in Rabbits

Despite their short lifespan and high reproductive rate, rabbits are not immune to fertility problems. The development of reproductive pathology reduces offspring production (size, number) and often has negative correlations with production efficiency. Hormones such as gonadotropin-releasing hormone (GnRH), luteinizing hormone (LH), follicle-stimulating hormone (FSH), estrogen, and progesterone are involved in regulating reproductive functions, and their impairment can reduce sexual interest and receptivity or even result in a complete absence of heat-a condition termed "anestrus" GnRH and other reproductive hormones are therefore crucial for stimulating normal reproductive cycles in rabbits. Although not frequently diagnosed, reproductive disorders such as ovarian cysts, uterine metritis, and endometritis require careful monitoring of mating behavior and reproductive performance, particularly in commercial populations. Corrective approaches may include improvements in diet or the addition of biochemical metabolites during times of increased energy demand, such as pregnancy, breeding, and lactation.

Reproductive pathologies affecting rabbits, particularly domestic breeds, have received relatively little attention compared with other physiological systems. Nevertheless, reproductive functions often require greater metabolic investment than other bodily activities. Financial losses are not restricted to immediate breeding failures; they also encompass subsequent production cycles, when uterine pathologies can impair embryo reception. All such morbidities reduce litter size and quality (weight). Potential biochemical pathways that affect reproductive performance remain understudied, partly given the complexity of carotenoid and lipid metabolism during oocyte, ovum, and spermatic fluid maturation. Promising avenues include the use of pro- and prebiotics, hormonal addition to diets, and the regulation of metabolic activity via vitamin supplementation [111, 112, 113, 114].

Hormonal Regulation of Reproduction

Reproductive physiology relies upon the interaction of hormones secreted by hypothalamus, adenohypophysis, ovaries, and uterus. Gonadotropine-Releasing Hormone (GnRH) stimulates secretion of Lutropine (LH) and Follicle-Stimulating Hormone (FSH), which promote development, maturation, and ovulation of ovarian follicles, spermatogenesis, and synthesis of estrogen by follicles. Estradiol induces heat, stimulates secretion of LH, and prepares uterine endometrium for gestation. After ovulation, follicles transform into corpus luteum, which during pregnancy produces progesterone to maintain gestation, repress sexual receptivity, and affect proliferation and secretion of endometrial glands. Reproductive physiology in buck can be briefly summarized, as follows: Gonaotropine-Releasing Hormone stimulates LH and FSH secretion; LH induces Leydig-cell secretion of testosterone; testosterone is necessary for spermatogenesis and development of repro ducts and secondary sexual characteristics. Reproduction can also be modulated using metabolic approaches: Nutrition directly influences production of the reproductive hormones through their precursors and also through insulin-like growth factors and total triiodothyronine levels.

Anestrus may arise from abnormal GnRH secretion patterns and can be treated by hormone therapy. Follicular cysts result from insufficient LH surge after estrogen peak and can be treated with human Chorionic Gonadotropin, ranging from 200 to 600 UI depending on the experiment. Uterine pathologies are frequent reasons for infertility and diagnostic indicators can include vulvar discharge, blood test (increased leukocyte number and decreased heterophil proportion), and transabdominal ultrasonography (hypoechoic tissue, increased echogenicity, echogenic fluid). Integrated modulation of metabolic pathways can help support fertility during lactation and gestation [115, 116, 117, 118].

Common Reproductive Disorders

Anestrus, identified as a failure to exhibit estrus in a normal breeding season, can be caused by various factors, including environmental extremes (heat or cold), illness, malnutrition (deficiency of energy, protein, trace elements, vitamins), endocrine diseases (insufficient or excessive hormone production), poor housing conditions (overcrowding), selection for non-synchronous breeding, and age. Clinical signs include the absence of a swollen vulva, lack of courting or mounting behavior, and vaginoscopy revealing a small vaginal lumen, normal uterine horns, and ovaries with no visible follicles. Diagnosis is confirmed when the absence of estrus occurs despite normal winter conditions and feeding. Anestrus can be treated by correcting the underlying causes and reinitiating normal housing and feeding conditions.

Ovarian cysts are fluid-filled sacs in the ovaries and represent a relatively frequent reproduction alteration in females, particularly in those subject to conditions of heat stress. Hormonal imbalance during temporally assisted mating contributes to cystogenetic processes. Diagnosis is made through clinical signs and palpation of large cysts. Young rabbits with small, asymptomatic cysts do not need treatment, while hormonal interventions are recommended for older rabbits. The application of GnRH permits a rapid return to heat and gestation, while the administration of ovocystinoll and any compound acting like a LH can cure ovarian inactivity and consequently cysts.

Uterine pathologies are often asymptomatic. Uterine cysts, various forms of endometritis, metritis, and diffuse endometritis can occur and affect rabbit fertility. Diagnosis relies on visual inspection of the uterus after operation. These lesions can be treated on a case-by-case basis. [119, 120, 121, 122]

Improving Fertility through Biochemical Approaches

Enhanced fertility may be achieved through biochemically driven interventions along nutrition, vitamin and mineral supplementation, hormone therapy, and metabolic balance restoration. Increased hormonal secretions, attainable through metabolic activators, have been proposed to counter persistently low fertility rates, which remain a global concern. Faster improvement of reproductive performance would consequently benefit rabbit meat production, anticipated to reach an output of 1628 million tons worldwide by 2030. Rabbit hypersensitivity (allergy-like symptoms) to environmental irritants, particularly in dermatological tissues, has also been recorded.

Nutrition undoubtedly exerts a marked influence on rabbit fertility. Experimental trials have established that vitamin A promotes uterine development, iodine enhances growth and reproductive performance, choline impacts behavior and fertility, vitamin C deficiency reduces conception rates, folic acid deficiency causes higher embryo mortality, and vitamin B6 supplementation improves reproductive performance in both does and bucks, the latter possibly associated with a role in steroidogenesis. Optimized luteal metabolism using an environmentally safe anti-diabetic drug increases levonorgestrel concentration during the termination of ovulation and has been proposed to enhance fertility in rabbits by improving hormonal balance. Abnormal uterine conditions such as uterine contents of excessive ammonia nitrogen, high levels of pathogenic bacteria, and abnormal values of malondialdehyde, glucose, and hormone concentrations are associated with rabbit infertility. Combined vitamin and mineral supplementation improves semen quality, though the response of mammalian reproduction to supplementation is not always straightforward. Consistent with numerous studies on domestic animals, excess cholesterol in the diet does not promote porcine reproductive performance. [123, 124, 125, 126]

Chapter - 12

Metabolic Disorders and Their Management

Energy imbalances linking feed input and body mass development are critical; alterations may induce under- or over-nutrition, compensatory growth, or metabolic disorders that compromise production rates and health status. Nutritional balance during growth is vital for overcoming other morphological, physiological, or environmental issues. Under-nutrition, the most common disturbance in rabbits, results from insufficient energy supply for daily maintenance, and may lead to starvation. Conversely, over-feeding can induce metabolic syndrome, characterized by insulin resistance, adipose tissue hypoxia, dyslipidemia, altered fatty acid profiles, oxidative stress, and systemic inflammation, all with detrimental effects on fertility, product quality, and animal health.

Another vital metabolic disorder of growing rabbits is metabolic syndrome, defined as a complex of metabolic abnormalities in sub-adults and adults. It is a risk factor for dyslipidemia, diabetes, reproductive problems, increased susceptibility to numerous diseases, and a shortened lifespan. The clinical pathophysiological mechanisms of metabolic syndrome remain to be elucidated. Recovery may occur on sustained hypoenergetic feeding, yet preventive measures are preferable. Feed and environmental imbalance are key to the development of metabolic syndrome; thus, specific prevention strategies have been suggested. These include: protein restriction before seven weeks of age; daily feed amounts limited to 80% of demand; generally-balanced diets that avoid excess calorie supply and limit highly palatable ingredients; floor-pen housing that prevents physical inactivity; and reduced temperatures below thermal comfort levels. [127, 128, 129]

Energy Imbalances and Growth Disorders

Both deficient energy supply and excessive dietary energy for fast weight gain can lead to adverse consequences in rabbits. Undernutrition during growth results in permanent loss of growth potential if feed intake is restricted for more than two-thirds of the growth period, whereas overfeeding is followed by undesirable metabolic disturbances such as metabolic syndrome. Catch-up growth after a period of limited feed intake is possible, although compensatory growth negatively influences feed efficiency. In a commercial setting, young rabbits are at risk for energetic imbalance early during the rearing phase or close to sexual maturity, while adults may be affected during peak reproductive performance.

Nutritional support for these different physiological stages should consider several metabolic disorders related to energy imbalance. Inadequate energy supply may result in fetal loss, increased post-partum interval, impaired milk production, and reduced weight gain of nursing kits, while excessive energy causes high rates of neonatal mortality, poor quality of kits, and reduced sexual performance. Routinely implementing biochemical analysis for monitoring energy level and related metabolic disorders should enhance economic efficiency in commercial rabbit farming. [130, 131, 132]

Metabolic Syndrome in Production Rabbits

Insulin resistance, altered lipid metabolism, and associated pathophysiological processes comprise metabolic syndrome, prevalence of which is on the rise in humans, pets, and an increasing number of animal species, primarily rabbits. The condition disturbs normal metabolic homeostasis and predisposes individuals to development of hyperlipidemia, hypercholesterolemia, and dysfunctions of multiple organs and systems. In rabbits bred for meat production, especially those housed in environments with elevated temperatures or exposed to chronic stress, metabolic syndrome is a condition of heightened concern because it negatively affects production efficiency and ultimately economic revenues.

Multidisciplinary approaches, which integrate knowledge and expertise across the fields of animal pathology, analytical chemistry, and physiological sciences, enhance the efficacy of studies in the domain of animal science. Various research efforts in different branches have revealed associations between metabolic imbalances during growth phases and abnormalities in feed composition and quality. Investigations exploring pathology in production rabbits have indicated relationships between pathological lesions and variables such as growth rate, feed conversion efficiency, weight gains, and mortality. An efficient methodology for controlling herd health and optimizing production efficiency involves collection and analysis of pathology, hematology, and clinical chemistry information. [133, 134, 135]

Prevention Through Diet and Environmental Control

Under- or overfeeding and diets unbalancing metabolic homeostasis can damage growth or predispose to diseases and metabolic syndrome. Well-crafted diets, with nutrient proportions satisfying physiological needs and the right energy density, avoid diseases. Disease-related deaths and production losses drop when metabolic functions are supported through periodical feeds, compounded by organic acids, minerals, or antioxidants.

Nutrition is a key factor in shaping rabbit growth dynamics; it becomes even more critical during periods determining metabolic development, such as weaning, and these critical windows of development, when permanent connective tissue scarring may ensue, can account for abnormal growth trajectories with long-term consequences on production efficiency and very high carcass and feed units prices. Be this an under- or overfeeding, ensuring logically calculated feeding schemes based on sex and pregnancy and avoiding a negative energetic status during lactation will mitigate gross production losses and metabolic disorders associated with energy imbalance. [3, 136, 137]

Chapter - 13

Integrating Pathological Findings to Improve Production Efficiency

Proper diagnostic data monitoring is crucial for effective herd health management. By gathering and analyzing information about health-related production parameters in a standardized manner over time, trends are detected, and herd status is assessed in relation to critical thresholds. Such an approach helps identify at-risk herds, connects herd health to productivity outcomes, and enables targeted interventions, thereby reducing mortality, improving growth rate, and optimizing feed conversion efficiency.

Given the significant impact of pathological lesions on production efficiency, it is important to correlate pathological findings with key performance indicators such as average daily gain, mortality, and feed conversion ratio. Investigators in different countries have established links between lesions on specific organs, such as the liver, respiratory system, digestive system, and reproductive tract, and their effects on growth, mortality, and feed conversion efficiency. These relationships aid in prioritizing health and disease prevention programs that directly benefit production parameters.

Analyzing histopathological data from rabbit farms and linking the results with production outcomes related to growth, mortality, and feed conversion ratio can facilitate a predictive approach to disease reduction. By calculating average daily gain and mortality for each barn or batch, calculating the average feed conversion ratio for each production cycle, and determining the number of animals with specific pathological findings at slaughter, diagnostic criteria levels can be established and provide a basis for effective prevention and control implementation [138, 139, 140].

Diagnostic Data for Herd Health Management

Systematized information, diagnostic tools, and databases are fundamental to herd health management, enabling timely, targeted disease control approaches. Veterinary diagnostics increasingly encompass histopathology, cytology, hematology, and molecular pathology. Disease lesions rarely manifest as single entities, necessitating integration of diagnostic data from affected and non-affected animals for productive disease management. Organ function tests, oxidative status assessment, and enzyme profiling complement histopathological and hematological findings and support practical herd health monitoring.

Hematopathology and clinical biochemistry provide composite diagnostic indicators of production rabbit health and correlate with growth, feed conversion, and mortality. Integration of such data can facilitate epidemiological maps of herd health status, in which established diagnostic thresholds for specific tissues or organs signal potential enteric, respiratory, or reproductive disorders. Data interpretation within a dedicated decision support system can enhance animal welfare, optimize investment returns, and ensure product quality in commercial settings. [2, 141, 60]

Linking Lesions to Performance Outcomes

Pathological examinations reveal lesions associated with poor production results. Establishing correlations between these lesions and three critical metrics-weight gain, mortality up to slaughter, and feed conversion ratio-enables interpretation with practical significance. Such analyses offer stakeholders insight into the implications of diagnostic outcomes, guiding decisions on herd health strategies and sector vitality.

Recent studies demonstrate that producer rabbits with pathological lesions exhibit slower growth, elevated mortality, and poorer feed-efficiency ratios. These findings underscore the impact of pathology on production performance, prompting further investigation into these relationships and motivating efforts to monitor herd health using pathologists' reports [3, 142, 143].

Predictive Approaches for Disease Control

Diagnosing diseases early favours recovery and renders therapies more effective. Traditional approaches target infectious and highly mortal afflictions. Adopting a broader perspective on disease control can preserve herd health and decrease production losses. A predictive strategy stratifies farms according to disease occurrence. Health and production parameters guide adjustment and maintenance of control measures, allowing warnings for emergent problems.

New pathologies and tumourigenic proliferations are appearing or surfacing in diverse species. Continuous mass production favoured by global trade increases vulnerability. Conditions promoting immunosuppression or structures facilitating high animal density enhance the impact of previously ignored infectious agents. At the same time, humans are invariably exposed to chronic subtoxic doses of various compounds. Consequently, it is not surprising that novel apathologies and infection-related lesions with low to null appeal are regularly reported. Nevertheless, a more thorough analysis might alert farmers to the potential emergence of those conditions in their own populations, allowing them to adopt preventive measures ahead of time. [144, 145, 146]

Chapter - 14

Innovations in Biotechnology and Analytical Chemistry

Molecular diagnostics, advanced analytical technologies, and smart monitoring systems enhance productivity by improving disease detection, risk management, feed and tissue quality, and preventative health maintenance. Techniques such as genotyping, transcriptomics, and metabolomics facilitate marker-assisted breeding, functional genomics, population diversity studies, and disease resistance forecasting. Recent advances in spectroscopy, chromatography, and sensor-based analysis enable rapid detection of feed nutrients and contaminants. In conjunction, real-time monitoring systems employing Internet-of-Things sensors detect changes in herd health status through follow-up analyses of ambient conditions, behavior, feed intake, and body-weight response.

Molecular techniques allow better management of potential diseases before they become endemic. Genotyping tools enable gene-based selection for disease resistance, whereas gene expression profiling uncovers candidate genes for trait enhancement. Analysis of metabolite profiles holds promise for early detection of infectious diseases. The use of population marker systems to locate quantitative trait loci facilitates more efficient improvements in desirable characteristics by guided selection. [147, 148, 149]

Molecular Diagnostics and Genomic Tools

Next-generation genomic tools enable genetic detection of major rabbit diseases, assessment of pathogen resistance in breeding stock, and selective breeding for dysbiosis-sensitive rabbits. Polymorphisms associated with resistance to rabbit viral hemorrhagic disease are detectable in non-Leucaena-fed rabbits. Progress in next-generation sequencing and gene expression profiling facilitates routine transcriptome analysis of poorly characterized diseases. Resistant and donor-population genotyping is now genome-wide and low-cost. Rapid, multiplexed single-nucleotide polymorphism scoring is available for seven major rabbit infectious agents. Genome-wide association studies of natural infections and transcriptomic characterization of developmental immunity are underway. Mapping introductions of rabbit enteric viruses and controls on dysbiosis-associated pathogens are also provided.

Recently developed cost-effective technologies for routine monitoring of rabbit feed and tissues include two-dimensional gas chromatography, high-resolution mass spectrometry, and novel optical sensing devices with nanomaterial technologies. Detections for major intracellular metabolites have greatly expanded. Dietary mycotoxins can now be screened in various tissues, and contaminators identified by machine-learning-based spectral interpretation. Key metabolites associated with particle size have also been proposed for physiological monitoring through smart monitoring technologies integrated into farm control systems. Advanced spectral detection of water-soluble vitamins is now rapid, low-cost, and multiplexed. Combined with systems biology, smart monitoring platforms can provide physiological diagnosis of farm animals in real time. [150, 151, 152]

Advances in analytical chemistry for feed and tissue Testing

Tissue and feed composition testing is essential for animal production but necessitated costly specialized laboratories with prolonged turnaround times. Progress in chemical analysis has enabled the development of rapid-field test systems widely deployed to detect feed-contaminating elements, nutrients, and other chemicals. Recent innovations involve miniaturized gas and liquid chromatographic systems and physical–chemical sensors linked to data-analysis networks.

Advances in analytics have made it possible to test tissue and feed composition directly in the field. State-of-the-art equipment developed over the past decade seeks to optimize and accelerate chemical analysis that is fundamental to animal production yet requires costly specialized laboratories. The novelty of these techniques is their ability to detect, identify, and quantify feed-contaminating elements, nutrients, and chemicals in a short time frame and with basic training. One of the most promising routes is the combination of ecological biosensors that use natural processes to recognize the presence and quantity of analytes, which react with colored or chemoluminescent pigments, coupled to physical–chemical sensors that measure changes in temperature, electrical conductivity, or pH, establishing multiple connections with data-analysis networks. [153, 154, 155]

Smart Monitoring Technologies for Rabbit Farms

Emerging Internet of Things (IoT) technologies enable continuous monitoring of environmental conditions, animal health, and production processes, facilitating rapid adjustments and risk reductions. Monitoring systems integrated with cloud data processing and analytics detect abnormalities and hazard exposures, alerting farmers to ongoing or impending problems. Such approaches enhance herd health, optimize resource allocation, and support eco-friendly production.

Wireless sensors monitor temperature and humidity, enabling bioinformatics analyses of heat stress in experimental rabbits. Temperature sensors assess thermal comfort in commercial breeding units. Airflow meters optimize ventilation. Real-time monitoring of CO_2, pH, temperature, and dissolved oxygen concentrations supports water quality management and health surveillance in fish farming. Automated 24-h measures of electrical signals, redox potential, pH, chemical oxygen demand, temperature, and ammonia concentration enhance aquaculture management. Cameras track behavior and detect individuals affected by epidemics. Airborne bioparticle levels are monitored to control herd disease risks.

Annual tissue and feed testing for mycotoxins, bacterial endotoxins, pesticides, and heavy metals characterizes biosecurity status. Multi-residue detectors for pesticides, growth promoters, and anabolic agents ensure safety. IoT devices for animal husbandry control feed quality and monitor meat freshness. [156, 157, 158]

Chapter - 15

Sustainable Production Systems for Enhanced Efficiency

Industry 4.0 technologies-e.g., intelligent sensor networks, advanced spectroscopic tools, molecular diagnostics-may increase production efficiency on rabbits farms by enhancing sustainable welfare-oriented housing, feed formulation, and pathophysiological management. Production systems designed to consolidate sustainability, set in harmony with the environment, can be genetically, chemically, and chemically balanced for maximum animal productivity. Data from suitable evidence-gathering programs offer stress minimization, humane handling, and therapeutic freedom to foster the comfort, health, and growth of caged animals.

An environmentally aware housing system limits negative climatic impacts through design, ventilation, exhaust gases, and waste management. Decreasing ammonia release in the surrounding environment, improving ammonia and dust concentrations, and lowering enteric methane emissions promote eco-sustainability. Ensuring temperature-dependent comfort within the rearing and fattening phases is fundamental to reducing production costs while enhancing product quality. At the farm level, the carbon footprint could be minimized through the use of dietary supplements aimed at decreasing enteric emissions. Production optimization through intelligent feeding paradigms-development of computer-aided diet formulation, with inputs from food chemistry, nutrition, and palatability studies: balanced diets with minimized mycotoxin contamination, combined with precautionary measures for toxin- or disease-contaminated sources-contributes to environmentally sound farming. An overall food occurrence in animal production aimed at supporting animal health, together with management procedures for enhancing productivity and welfare, translates into human safety for the consumers. [159, 160, 161]

Environmentally Conscious Housing Systems

Housing design and ventilation are crucial in rabbit production, as suboptimal conditions stress animals and increase disease risk. The aim is to develop an environmentally conscious housing system that integrates optimal ventilation with robust waste management.

Housing systems influence animal health and well-being, production efficiency, and climate change. Welfare-deteriorating conditions-such as thermal discomfort-stimulate stress hormone production and decrease feed intake, ultimately impacting growth and reproductive performance. Proper housing design also mitigates parasite and disease exposure and reduces the need for veterinary inputs and therapeutic drug residues. Furthermore, optimized dung storage conditions prevent environmental pollution. The housing system should therefore balance ventilation, animal comfort, and waste management to create an environmentally conscious solution.

Different ventilation types, including natural, mechanical, and hybrid systems, can be employed in rabbit production. Annual cost-benefit analyses are essential in selecting the most appropriate type. Houses should be designed, oriented, and equipped with wind shields and aeration devices to enhance motivation toward feed intake despite unfavourable climatic conditions. Planting shade trees around the housing and providing clean, cool drinking water during periods of high ambient temperature also help reduce thermal load. Optimal stocking density and innovative cooling methods are further strategies for preventing heat stress.

Dust, ammonia, and hydrogen sulfide concentration levels, as well as respiratory disease incidences, can be reduced using adequate ventilation systems. Such systems-combined with the segregation of different categories-are the most feasible way to minimize ammonia pollution and erosive dust concentrations, particularly in extensive rabbit productions. Optimal maintenance of rabbits in winter and summer in combination with fly control is also recommended.

In summary, environmentally conscious housing systems for rabbits should be enabled by adequate ventilation provision, appropriate environmental conditions, strategic husbandry practices, and proper combined waste management. [162, 24, 163]

Chemically Balanced Feeding Strategies

Animals revolve around the regular intake of feed to supply growth and maintenance requirements. Data from farm animal production indicate that feed typically represents over 70% of operational costs. The expected profit margins result from the difference in selling and acquisition price, meaning that small increases in feed production cost are directly translated into a proportional loss of profitability. That illustrates the importance of feed formulation, requiring a decreased feed cost and improved feed efficiency. Chemically ad balanced rations positively impact chemical cues, animal growth and health, reproduction rates, and productivity costs. Formulate rations with chemicals at levels that favour animal growth and metabolism without alteration of the organs that digest and assimilate the nutrients. Animal diet composition directly influences feed consumption dynamics and nitric-oxide metabolism, with consequences for oxidative damage, cell proliferation and hormonal secretion.

Ovulation rate and litter performance improve with hormonal induction using LHRH, while litter size at weaning responds to metabolic hormones. A high-protein diet in breeding females and nutritional support for breeding males boost reproductive indices. Clean and adequate housing, avoiding excessive temperatures, high humidity and ventilation, strass, ammonia gas, and overcrowding guarantee better reproductive rates. Enhancements in litter size and weight at birth and lower mortality are obtained with added bioactive compounds. Chronic exposure to low concentrations of certain pollutants from industrial or agricultural sources causes metabolic disorders, and it is crucial to monitor farms for the presence of hormonal active substances. [164, 165, 166]

Welfare-Oriented Pathophysiological Management

Animal welfare plays a key role in production systems because it determines animal health, feed utilization, growth patterns, disease resistance, reproduction, and product quality. Pathophysiological management focuses on supporting animal welfare through stress reduction and humane handling, while simultaneously preventing pathological conditions and promoting health-supporting environments. Stress disturbs homeostasis and compromise both the entertainment and productivity of animals. Well-designed housing systems and breeding practices contribute to a healthy and positive environment while minimizing aggressive competition among animals.

Stress can originate from external environmental factors (heat/cold, humidity, dry air, dust, ammonia, chemicals), endogenous factors (metabolic syndrome, hormonal imbalances), and inadequate housing and breeding practices. All these factors lead to increased cortisol and catecholamine secretion. In addition to being the stress-response hormones, cortisol and catecholamines stimulate gluconeogenesis, insulin resistance, lipolysis, and lipogenesis. These hormonal actions modify the acquisition and utilization of nutrients, complement the therapeutic response to infections, and assist in adaptation to environmental changes; however, their excessive secretion has adverse effects on feed intake, digestion, metabolism, and growth. Therefore, an optimal balance in hormone levels during the different phases of production is important for animal welfare and economy. [167, 168, 169]

Chapter - 16

Future Perspectives in Integrative Rabbit Research

Integrative study of pathology, chemistry, and rabbit physiology to improve animal production efficiency: present an objective, evidence-based, formal analysis with clear, scholarly language.

Herd health, food contamination, animal welfare, and the conservation of natural resources at all levels continue to stimulate research. In rabbit production, pathologies, chemical hazards, and ecological factors are core themes for attention. Affected populations must be monitored using current methodological platforms. Technologies for maggot debridement and mosquito control require further evaluation and FDA approval. To mitigate contaminations, the development of detection methods based on biosensors or other advanced analytical procedures is promising. New insights into dopamine receptors are likely to enhance management practices. Chemical additives, particularly probiotics and prebiotics, can be employed to improve rabbit productivity and quality.

Molecular diagnostic techniques such as genotyping, sequencing, gene expression profiling, and the determination of disease-resistance biomarkers should be incorporated into rabbit population analysis to support breeding strategies and epidemiological surveillance. Genomic Information offers opportunities for the early identification of resistant individuals in experimental infection models. Novel molecular tools for feed monitoring and animal-health assessment are emerging in the areas of bio-sensing, nano-biosensing, RFID, and data-analysis technologies. Such devices can now be implemented in the field to provide practical indications for the surveillance and control of rabbit health. [170, 171, 172].

Integrative biology research has gained significant attention in recent years, owing to its multifaceted analysis of biological systems across multiple levels, from DNA to organism. Comprising an integrated multiscale architecture of biological systems and their functional interactions, the approach has broad applicability in agriculture, animal science, and biomedical research [1]. A shift from quantitative to integrative biology has become evident at the University of Ljubljana over the last two decades, focusing on important traits such as growth, fat deposition, and disease resistance in pigs, rabbits, and fish.

Integrative biology combines genomics, transcriptomics, epigenomics, proteomics, metabolomics, and phenomics within a systems framework. Efforts to advance this field include genome builds for rabbits, pigs, and fish, the development of animal models through genome editing, high-throughput phenotyping, and the establishment of repositories for genetics, expression, and phenomic data. Domestic species provide extensive datasets and information for blueprinting complex systems. Consequently, expanding integrative biology within rabbit and other anima models could offer crucial insights into human health, welfare, and the development of new treatments.

The rabbit constitutes a valuable, yet underutilized, model organism for genomics, physiology, and translational research. Initial groundwork establishing the rabbit as a bio-analogue to humans completed several decades ago; however, a comprehensive framework integrating genomic and physiological information, biomedical knowledge, and quantitative methodologies remains to be developed [1]. This oversight persists despite the growing interest in the rabbit as a model for the study of various diseases, including cardiovascular, pulmonary, neurological, metabolic, and infectious conditions [2] , particularly for conditions considered analogues in humans and animals. Complementary advances in sequencing technologies and genome editing further elevate the rabbit's translational potential by offering opportunities for faithful modelling of human diseases, high-accuracy genome, transcriptome and epigenome editing, and the generation of multi-omic datasets.

Although research spanning the integration of these domains is scarce, multiple preparations-with varying constituent components, complexities, and integration approaches-are already available. For instance, basic datasets such as the rabbit genome and annotated rabbit genome sequences aligned with other species exist. Modelling configurations exploring unveil disease mechanisms-some of which model conditions directly associated with human diseases capable of calibrating preclinical-to-clinical translational rates-or simulating biological features, interactions and metabolic networks of organisms corresponding to human relevancies have also been established. Solutions specifically targeting rabbits, incorporating information exclusively on this species, and generic preparations merging multi-species details are both accessible.

Significant advances in rabbit genomics and biomedicine stimulate renewed efforts to explore their integrative potential. Genomic editing techniques now support the development of highly relevant disease models [3]. Physiology closely parallels that of humans and other species across key dimensions, enabling translational studies in both human and veterinary contexts. Synchronized multi-omic profiling capabilities feed comprehensive system-wide analyses. Physical-activity measurements and imaging methods such as magnetic resonance, ultrasound, and positron emission tomography further augment high-content phenotyping by adding time-varying, spatiotemporal, and multimodal information.

Technological advancements widen the scope for integrative studies across a diverse range of phenomena. Genomic editing via CRISPR/Cas9, bacterial artificial chromosomes, and piggyBac systems underpins model creation, with corresponding strategies for knockout validation safeguarding experimental reproducibility. Physiological correspondences with human disease models encompass infectious, inflammatory, metabolic, and oncological conditions. Well-studied diseases occurring in multiple species provide clear entry points for translational exploration.

The rabbit has emerged as a valuable animal model for biomedical research, with the development of new approaches that allow genomic editing to generate preclinical models of human disease. Precise genome editing techniques have advanced greatly in rabbits, with the CRISPR/Cas9 system having been successfully established as a reliable platform for rabbit gene editing. The availability of reference genome sequence, together with the potential to generate knock-in and knock-out (KI and KO) mutants, has greatly facilitated the establishment of rabbit models of human diseases for research and therapeutic purposes. Editing genome was shown to be precise and devoid of undesired mutations. Further innovations, including the development of transgene-free gene targeting and multiplexed genome editing strategies, will further broaden the application and improve the efficiency of genome editing in rabbits and enhance their attractiveness as translational models [3].

The rabbit exhibits numerous physiopathological features that mimic human diseases, rendering it a valuable interspecies model of human physiology and a vital biomedical analogue [4]. This section summarizes key rabbit physiological characteristics and their respective analogues among veterinary species and humans. Rabbit physiological parallels with veterinary species are outlined, followed by those shared with humans.

The rabbit has long been recognized as an important biomedical model in many disciplines, including cardiology, gastroenterology, pulmonary and osteoarticular physiopathology, pharmacology, and toxicology [2]. Robust cardiovascular and pulmonary system knowledge aids evaluation of cardiovascular and respiratory physiopathology. The rabbit is particularly well-suited for studying cardiovascular diseases such as hypertension and atherosclerosis, as its arteries and veins are larger in diameter and their composition more comparable to humans than in other small models; blood pressure and heart rate are also similar to humans. The rabbit's gastroenterological system is extensively studied, and rabbit models are widely used to investigate enterotoxic shock and therapeutic approaches to intestinal transplantation. The rabbit osteoarticular system is well characterized, and all parameters used for rheumatology are available, including the Carrageenan and Freund models of arthritis and the development of osteoarthritis and osteoporosis. Ocular diseases such as keratitis, uveitis, cataracts, and glaucoma have a high socio-economic impact; an extensive array of in vivo rabbit eye models has been developed.

In veterinary medicine, rabbit dysbiosis is one of the most important risk factors leading to gastrointestinal stasis, resulting in severe clinical signs and often death. Gastrointestinal stasis in rabbits shares aetiological, clinical, and paraclinical similarities with enterotoxic shock in humans, suggesting high translational potential for enterotoxic shock research. Research into the aetiopathogenesis of keratoconjunctivitis sicca-one of the most common ocular complaints in pet rabbits, particularly the Netherlands dwarf breed-has clarified the roles of meibomian gland dysfunction and increased tear evaporation. Kerato-conjunctivitis sicca is also a frequent focus in human ophthalmology, particularly regarding dry eye syndromes (déficit lacrymal et séquelles des déchirures). Further studies on keratoconjunctivitis sicca in rabbits are warranted for aetiopathogenic investigations and the evaluation of therapeutic strategies.

Over the past two decades, science and technology have seen unprecedented development, yet the core methodologies used to study living organisms – namely, genomics, transcriptomics, proteomics, and metabolomics – remain the same. These methodologies constitute the foundation of systems biology and serve as the basis for the development of causal biological models. Two main technologies are necessary to study the fundamental life processes governing organisms: observable macromolecules and signals (e.g. chemical signals) and perturbation-inducing interventions (e.g. chemical stimulation). The crucial technological processes of real-time in situ imaging and high-throughput perturbation are still beyond reach, rendering life processes an "unobservable black box." The lack of effective tools for science to study life limits the exploration of life processes and, in consequence, hinders human understanding of life. The rabbit is becoming a unique experimental animal model with unprecedented potential to expand above-mentioned science. The rabbit and human, as long mammals, share great physical similarity and molecular homology in the genome, transcriptome, and proteome level. Rabbits can be applied to study wide range of human disease including but not limited to hypertension, atherosclerosis, bone disease, autoimmunity, virial infection, cancer et al., giving it the title of "Non-rodent Mammal Model". But as the numbers of research on rabbit remains to be few, the rabbit science is still at the very basic level. The system biology scientific study on rabbit needs incorporation with multiomics modeling. Various experimental intervention-altering approaches, including transgenic, model establishment, and drug stimulation can be integrated to the study and different drugs can be annotated and correlated to the human disease. All these works, a keyword search will lead to massive raw resource with a direct needs of data integration.

Systems biology encompasses a variety of approaches that enable comprehensive analysis of biological systems by integrating diverse datasets-genomic, transcriptomic, epigenomic, proteomic, metabolic, phenotypic, and imaging data in particular-at different scales of organisation [5]. Causal inference complementary to network analysis and simulation-based modelling further extends the range of conceptual and analytical tools available to integrate experimental and observational data across heterogeneous data domains. Systems biology facilitates the characterization of complex biological systems and phenomena by capturing emergent properties at the system level and elucidating the underlying behavioural rules and mechanisms-the insight cannot be gained through reductionist analyses of individual molecules or even molecular networks and pathways [6]. The adoption of a systems-based perspective thus offers innovative and incisive means to address fundamental questions at the interface of rabbit biology and biomedical science.

Systems biology represents a paradigm shift from reductionist to systems-oriented analysis; despite being applied extensively to other species, its potential for integrative rabbit research remains largely untapped. The systems biology approach includes network analysis, simulation modelling, and data integration across genomic, transcriptomic, and phenotypic datasets; multi-omics datasets; and experimental and observational data on biological signalling and system behaviour throughout life. Causal inference is increasingly integrated into network analysis and simulation modelling [7]. Consequently, architectures are feasible for integrating a diverse, multimodal spectrum of data relevant and informative to rabbit research.

Multi-omics technologies-genomic, transcriptomic, epigenomic, proteomic, and metabolomic-enable comprehensive life-system characterizations at various molecular levels. Information from these high-dimensional, heterogeneous data layers can be combined to explore correlations, directly or indirectly connect causes and effects, and identify hierarchical control relationships. Specifically, if measurements are made in related phenotypes and regulatory relationships are inferred from other sources, the causal direction can be specified. Such integrative approaches have become popular owing to their potential to unravel biological mechanisms underpinning homeostasis and diseases in mammals and other vertebrates.

Progress in several areas is crucial for routine implementation of multi-omic studies, including development of (i) specialized data integration platforms, (ii) joint normalization resources to RNA-seq, proteomic, methylomic, and metabolomic profiles, (iii) pipelines for merging others' transcriptomic, proteomic, and metabolomic data with normed multi-species transcript-to-translated-protein-matched RNA-seq profiles, and (iv) analysis workflows for cross-species transcriptomic- or proteomic-projected phenome-wide association studies. Joint use of data from multiple layers and modalities can also yield improved definitions of biological parameters and traits.

Recent advances in imaging modalities for rabbits (e.g. MRI), coupled with improvements in high-content phenotyping, enable studies of physiology and disease progression over time. Key parameters include body weight, growth rate, organ weight, circulating biomarkers, and tissue morphology, as well as multi-omics data on gene expression and metabolomics. High-resolution imaging techniques provide access to parameters that correlated with the course of pathology in different rabbit models. These innovations offer the opportunity to perform longitudinal studies under controlled experimental conditions and controlled environments, applying and adapting integrated systems analysis approaches already developed for rodents [3].

During the last decade, both clinical and experimental imaging methods have been developed for an increasing number of animal species, guided largely by the search for alternative species to rodents or monkeys for specific human applications [8]. Consequently, several groups have improved imaging techniques for the rabbit, broadening the spectrum of pathologies that can be studied in this model. The first in-vivo imaging of the rabbit (using µPET) predates the corresponding technique for the non-human primate by about a decade, and is certainly the oldest in-vivo small animal imaging available for large mammals.

Pre-clinical disease modeling has primarily benefitted human health and splitted into diverse fields and specialties with rabbit models offering advanced options. Integrative rabbit research forms a bridge between disciplines and can inform on the origin, management and treatment of communicable diseases with specific relevance to zoonoses. Consequently the rabbit occupies a unique, high-priority position in integrative research addressing societal challenges relevant to animals and human health alike. Ongoing rabbit models in genomics, physiology, population biology, monitoring of health and pest management span complex societal and public health challenges, ranging from emerging zoonotic communicable diseases in animals and humans through invasive modelling species and monitoring of weed species and animal pest management down to climate variability modelling impact.

Veterinary practice and rabbit welfare are ever important and should be included in future integrative rabbit research. Both aspects can benefit from collaboration with other laboratories and disciplines. Yet, establishing an integrative framework addressing these aspects is still premature and raising awareness of their significance constitutes a more immediate objective.

Rabbit welfare, popular as companion animals and increasingly used as models for human diseases remains unsatisfactory. The annual number of veterinary visits for pet rabbits is 18 times lower than for cats. Rabit vaccination, a low-cost and routine treatment in other species, is often omitted. Only 43% of pet owners believe rabbits possess mental abilities exceeding those of reptiles or fish, and explain accordingly rabbit care and environmental needs [9].

Due to anatomical and physiological similarities with humans (e.g., respiratory tract anatomy, heart physiology, eye structure), the rabbit is a relevant animal model for preclinical studies applicable to both human and veterinary health [2]. Conditions such as cardiovascular disorders, diabetes and obesity, dietary impact on health, and glaucoma attract increasing attention on the rabbit model, which holds its own unique signaling pathways and organs that provide insight into pathophysiological processes and system interactions. The various levels of genome, transcriptome, proteome, and metabolome provide a reference for understanding cellular circuits in human and veterinary health. Moreover, there are current efforts to develop rabbit-specific and cross-species bioinformatics and toolboxes, in order to facilitate multi-omics longitudinal studies on rabbit at broader spatial and temporal resolutions, respectively.

Investigation into ethical, legal, and social considerations is essential for the responsible and sustainable advancement of integrative rabbit research. Empirical evidence suggests that social-science insights profoundly influence stakeholder perceptions of, and support for, research involving animals [10].

Those engaged with, affected by, or responsible for research activities must therefore be at the center of corresponding inquiry. The welfare and conservation of rabbits may well serve as guides toward more generic principles, competent under international law, that encompass the full spectrum of laboratory animal species, including used, enjoyed, and relatively neglected ones [11].

In vitro and organ-on-a-chip rabbit models are emerging as promising alternatives to conventional animals. Organ-on-a-chip technology advances the development of physiologically relevant experimental platforms for understanding organ-level responses. By mimicking physiological conditions pertaining to health and disease (pH, temperature, shear stress, etc.) and creating stimuli-relevant environments (flow, oscillation, etc.), organ-on-a-chip in vitro models can help to predict the efficacy and safety of new biological entities or drugs. Given an increased understanding of human biology (genome sequencing, transcriptomics, epigenomics, etc.) and the success of the Human Cell Atlas project (https://www.humancellatlas.org), modelling human tissues and diseases through organ-on-a-chip approaches holds strong potential for impactful rabbit-related activities. Further information is available in the Livestock chapter of the ASP Program.

Computational modelling and simulation platforms are also developing rapidly throughout biology and medicine. Simulation aims to mathematically model the functionality of systems ultimately for predicting the response of the system to various scenarios. These endeavours can be from abstract (chemical reaction based) to concrete (physiological) modelling. Generally speaking, abstract models aim at universality where widely different experimental scenarios can be simulated by appropriately adjusting the meta-parameters of the model (such as cell numbers, binding rates, etc.) while concrete models aim not to reach universal predictions rather reproduce detailed experimental observations and enable extrapolation to the future. The modelling of interest in rabbit research arises when simulators reach some degree of abstraction and biological data may be collected elsewhere in animals such as mouse or human without being constrained to the experimental apparatus of origin. For rabbit, a high-dimensional description of the cellular dynamics of the immune system has been constructed based on general principles where only cell concentrations remain to be adjusted from the various species of the living system.

Further details are integrated into the corresponding proceeds of the ASP Workshop.

[3, 12]

To complement in vivo approaches, the development of rabbit-based in vitro methods is highly beneficial. These models facilitate early-stage studies, allow the examination of tissues at the cellular level, and provide an opportunity for high-throughput assessment. A series of commercial kits have emerged that allow rapidly growing rabbit cell lines to be cultured [13]. Toward further enhancement of organ-specific studies, research is underway to generate rabbit iPS cells, which could eventually lead to an organ-on-chip system specifically designed for the rabbit.

In the absence of stable inbred or genetically modified rabbit strains, the use of organ-on-chip technologies integrated with computational models provides in vitro alternatives for modelling rabbit physiological responses to drugs, chemicals, and diseases. Organ-on-chip devices have been developed for various organs and are gaining popularity due to their potential to recreate tissue architecture and functionalities while remaining amenable to high-throughput experimentation [14]. For rabbits, organ-on-chip replicas for the heart, skin, carotid artery, and liver are already available commercial systems. High-performance organ-on-chip technologies are widely accessible and stand to benefit rabbit research considerably.

Computational biology aims to describe biological phenomena at different levels, ranging from cell to organism, helping to understand the relationships between cellular networks and tissue or organ functions. In systems biology, mathematical and computer modeling aids in the study of biological networks and complex systems, distinguishing key genetic components and mediating signalling pathways [15]. Physiological-based computational modeling enhances the understanding of cellular interactions and their impact on tissue and organ function, being valuable for investigating health complications and testing therapeutic strategies [16]. Different types of models, either deterministic, stochastic, discrete, or continuous, can be developed depending on the biological phenomenon of interest, with increasingly complex approaches requiring integrated data from multiple models. An extension, called virtual twin technology, permits the integration of models describing different biological phenomena into a single platform.

Numerous modeling platforms, such as OpenSim (https://opensim.stanford.edu), Virtual Physiological Human Physiome Model (https://www.vph-share.eu), and multiscale musculoskeletal modeling (Tegnér 2009), focus on human physiology and anatomy through mathematical systems. Models incorporate simplifications of the human body to enable mathematical solutions in a reasonable time, acknowledging the lack of a widely accepted rabbit model able to replicate human pathophysiology and anatomy. The collection and analysis of multicentric databases covering population and individual-level parameters are crucial for developing animal-adapted modeling platforms.

Integrative rabbit research faces scientific, technical, and conceptual challenges that hinder its broader adoption by the research community and its prompt application to address critical issues in both veterinary and human health. Further clarification of the definitions of core concepts, systemic dimensions, and computational tools along with concrete examples can significantly simplify the adoption of this yet innovative approach. In addition, empirical support is necessary to build confidence in the proposed methodology, increase understanding of output interpretation, and facilitate wider acceptance. Four substantive areas stand out where collective efforts can achieve major advances.

First, there is a need to provide a more exhaustive overview of advancements in biomedicine concerning rabbits. Integrative frameworks combining data from rabbit physiology and disease with parallel omics information from humans should be established, drawing on existing genomic and breeding lineage knowledge. A compelling overview could cross-validate rabbit models that are translationally relevant to cardiovascular disease, diabetes, obesity, osteoarthritis, and respiratory disease, and yet under-utilized. Furthermore, extensions to high-dimensional imaging modalities, multi-infarct-generation, long-term multi-species longitudinal datasets, and computer-simulation platforms could bolster the plethora of directions in which the rabbit model is fruitful [2].

Second, the rabbit community could document the extent to which advancements in genetics, genomics, breeding, epigenetics, metabolomics, and other areas empirically establish a link between rabbit physiology and parallel perturbed states in either humans or rodents - thereby facilitating a highly portable extension of reverse-engineering approaches from existing rabbit datasets. Such empirical clarity and quantitative generative mapping would help delineate the specific hypotheses that can be explored within rabbit datasets, provide additional traction to modelling efforts, and link physiologically-hyperfocusing rabbit datasets to major social-media platforms showcasing phenomenology and mechanistic knowledge across mammalian species. A particular opportunity lies in documenting the overlap of human/rodent-cardio-metabolic physiology with rabbit datasets based on comprehensive human/rodent-multi-omic-others perturbation; yet such rabbit benchmarking has not appeared in the literature [17].

Rabbits represent critical scientific models for cardiovascular, osteoarticular, biomedical, and veterinary research [2]. Integrative studies would align with: (i) establishing differing prescriptions for veterinary care and (ii) advancing personalized food supply negotiations pertinent to dietary or obesity concerns. Furthermore, producing genetically-edited disease models would support preclinical studies for diseases affecting both domestic rabbit stocks and humans. Addressing companion animal welfare remains one of the top-three veterinary priorities in numerous European countries [17].

Integrative rabbit research provides opportunities to advance basic and applied knowledge in genomics, physiology, and translational biology. A fundamental goal is to characterize the genomic and physiological basis of complex traits and predict their responses to genetic manipulation and environmental perturbation [1]. Research questions motivate a systematic exploration of translational medicine using anesthetized New Zealand White rabbits for preclinical assessments of novel therapeutic modalities, drug delivery systems, medical devices, and surgical interventions [2]. Supporting aims include characterizing biopharmaceuticals and the corresponding tissue models, chronic wound models as functional surrogates for human diabetic foot ulcers, the relationship between electrocardiogram, blood pressure, and the onset of arrhythmia;

and establishing an adequate rabbit model for the study of the epigenome..

The rabbit genome sequence and analysis of its variations offer opportunities for rabbit genomics and genome-assisted breeding. As indicated by the availability of other high-quality annotated genomes, the rabbit model is prime for genomics, integration of multi-omics data with the corresponding modelling, characterizing of genome–environment interactions, and genetics of complex traits. Integrative rabbit research fits into a wider research context associated with multi-omics, with the expectation of accelerating discoveries in rabbit science and satisfying a growing need to rejuvenate the use of systems biology.

Emerging Pathologies and Chemical Risks

The analysis of contemporary rabbit production systems in light of emerging pathologies and environmental challenges has important implications for animal welfare and consumer safety. Production systems must be sensitive to and anticipate challenges caused by new infectious diseases and increasing levels of mycotoxins in feed. Such challenges can differ among production areas and seasons; their main effects should be identified to allow the most affected production characteristics to be prioritized for research. Attention to these factors will help maintain high animal welfare and prevent the release of unsafe food onto the market.

Abolition of rabies vaccination has been linked to disease recurrences, and viral zoonoses are poised to extend geographic distribution beyond their endemic range. The risk of transporting contaminated feed over long distances has increased recently with the growing exchange of compound feed formulations among producers. Ingredients for these feeds are often sourced from inhabited regions of Eastern and Southern-European countries, where climatic conditions favor fungi and mycotoxin contamination, particularly of cereal and fruit by-product components. Country/season oriented research is therefore needed to identify data gaps among specific groups of animal traits-health, feed conversion, reproduction-so they can be addressed holistically within viable time-frames. Prioritization enables a more thorough approach, with diagnostic input focused on those thresholds associated with changes in the key target trait factors, taking extra precaution where animal and food safety are at risk. [173, 174, 175]

Holistic Models for Physiology-Based Production

Physiology forms the foundation of every species as the basis of successful growth models, whether for fish, poultry, cattle, sheep, goats, or pigs. Yet, few production systems adopt these principles for the rabbit. Such models require ongoing operative research with a short time frame, integrating knowledge from different domains to exploit natural advantages through chemical feeding, adaptive biochemistry, immunological protection, and stress reduction.

With numerous modern livestock production problems linked to pathology, metabolic chemistry, and physiological adaptation, combined knowledge should improve their management. Despite sharing similar biochemical and immunological responses with poultry, abnormal lesions in rabbits are rare in embryostics but commonly detected postnatally as atrophy, degeneration, apoptosis, inflammation, infection, or metabolic errors. Pathological analysis can clarify relationships among lesions, blood biomarkers, and growth indicators, including efficiency, mortality, and feed conversion. Integrating chemical and physiological knowledge offers opportunities to enhance productivity [176, 177, 178].

Integrating Science and Technology for Next-Generation Efficiency

Cross-disciplinary platforms and translational pipelines are needed to harness biotechnological innovations and address the emerging issues constraining rabbit production. Rabbit farming is a pioneering domain in the convergence of agrotechnology and biomedicine. Consequently, it may benefit from advances in area-specific biotechnology, pathology, and animal chemistry to consolidate successful outcomes. Research efforts addressing various domains should, therefore, converge to enhance the benefits of biotechnological innovation.

Particular attention must also be paid to chemical hazards and stressors. The dynamics of contemporary society are favouring excessive chemical enhancements in the environment. Thus, new paradigms in veterinary pathology and toxicology are emerging, reinforced by enhanced analysis techniques. Rabbit production is not immune to these events, meaning that some operators may now be exposed to conditions that metabolic pathways did not encounter during the previous 4000 years. As a result, subtle bodies' adaptations may also appear, leaving the sensory nervous system unaware of any imbalance and allowing the gradual evolution of new disorders associated with chronic subclinical toxicological effects. It is crucial, therefore, to understand the recent conditions of exposures to better prepare against the unknown and mitigate the consequences. In short, science can help the rabbit industry to overcome current constraints and future limits. [5, 7, 179, 180, 181, 182]

Chapter - 17

Conclusion

Analyses from the fields of veterinary pathology, analytical chemistry, and both systemic and functional rabbit physiology converge to provide management pointers that can enhance rabbit production efficiency. The integration of diagnostic, metabolic, and physiological evaluations opens avenues to improve production metrics. Organ condition monitoring and post-mortem inspection form historical baselines useful when interpreting future pathology findings. Characterizing associations between common pathological changes and rabbit production outcomes further assists management by highlighting risk factors and biological targets for optimization. Finally, combining diagnostic data into a central dashboard enables timely herd health management and corrective action.

Rabbit production is continuously challenged by increasing economic pressure, growing consumer demand, more stringent animal welfare requirements, and concerns regarding the use of antibiotics and other chemicals in food production. Increased morbidity and mortality, and the high variability in production performance, are serious impediments. Advances in modern veterinary pathology, metabolic research, and functional studies of the rabbit offer opportunities for a more efficient rabbit production system. These fields of rabbit science contribute new disease-related knowledge, chemicals acting in the feed or animal, and the physiological basis for metabolism. Integrating these different approaches will provide the basis for a deeper understanding of production efficiency and ultimately offer evidence-based recommendations to optimize rabbit husbandry.

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