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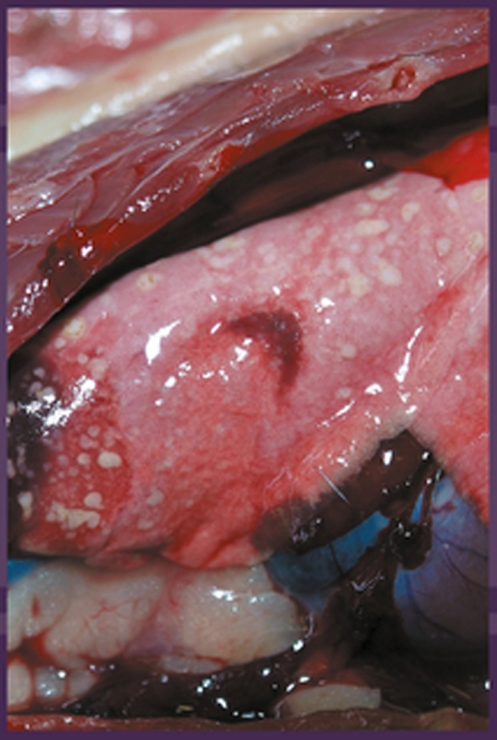
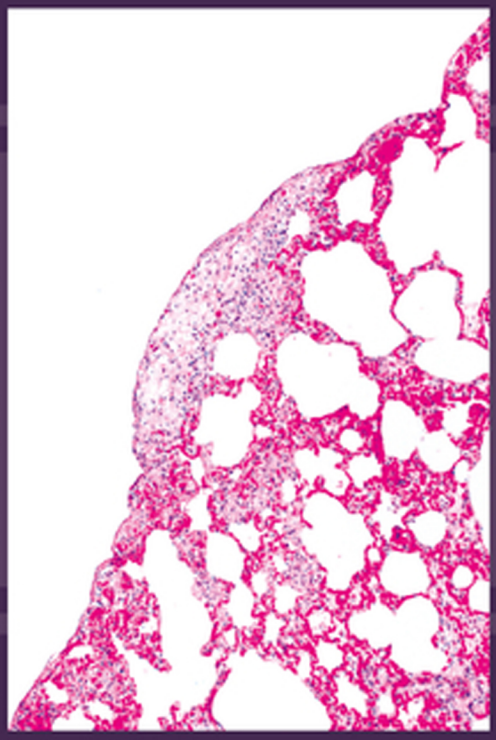
Patricia V. Turner, Marina L. Brash
and Dale A. Smith





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Preface

Pathology of Small Mammal Pets provides current information on congenital abnormalities, spontaneous and infectious diseases, degenerative and neoplastic conditions, and incidental findings for a range of popular small mammal pets. We have not attempted to be exhaustive in content, since there are excellent, well-established resources available already for laboratory rabbits, ferrets, and rodents, but instead have taken a practical, systems approach to conditions likely to be seen predominantly in companion animal settings. We have supplemented this with relevant information for breeding operations, including pet store suppliers as well as facilities breeding small mammals for food for other species, and, in the case of rabbits, for commercial meat rabbit production, as it is next to impossible for veterinarians to find information on these groups of animals in traditional veterinary medicine and pathology publications. Where information is available, we have also addressed herd or colony management strategies for various conditions, again, recognizing that it is often not enough to have a diagnosis in hand to provide optimal client support and patient care. Veterinary expertise in animal health management can readily be transferred following a review of species-specific information found in this book. It goes without saying that the public health responsibilities of veterinarians and veterinary pathologists extend to these small mammals in all the settings in which they are commonly encountered.

This book is intended primarily for veterinarians, veterinary pathologists, veterinary technicians, and veterinary students, but it may also be of interest to animal owners, breeders, and producers. Although there is much more work to be done in this field of practice, knowledge of small mammal diseases, interest in small mammal medicine, and availability of high quality veterinary care for these species have grown exponentially over the past decade. The increased popularity of small mammals as pets may reflect increased urban dwelling and a need for people to engage with animals in a more compact environment. Small mammal clients are often very knowledgeable about their animals and have high expectations for quality veterinary support to improve animal care and well-being.

We were inspired to take on this project close to a decade ago by a colleague and mentor, Dean H. Percy, who reminded us on more than one occasion of the glaring gap in the literature. As is typical for many books, what began as a casual hallway conversation morphed into a full-fledged effort. It has been a long and interesting journey, and we hope that the information gathered within this volume will be of use to fellow veterinary colleagues. Small mammals are charming and fascinating animals to work with and we hope that this resource will be used as a means to enhance their care. Despite our best efforts and given the continuing evolution of knowledge in this field, we know that there will be errors and omissions, and we invite readers to provide suggestions for correcting and improving this work.

Acknowledgments

We are grateful to our colleagues who work in veterinary practice, diagnostic laboratories, and as private consultants for sharing their expertise during the preparation of this book. Small mammal pathology cases are not seen routinely in many diagnostic laboratories thus it can be difficult to develop clinicopathologic correlates to ensure continued learning for veterinary clinicians and pathologists alike. Publication of case reports in meetings proceedings and journals is essential for improving the quality of care for patients and service to clients. Case reports are often not credited sufficiently in academic settings, however, without these publications many conditions affecting small mammal pets would not be formally documented.

We would especially like to recognize the support given to us by our families. We owe a special debt to Fabio, Allan and Betty, Ken, and Brian who have indulged us repeatedly over the years to make time for this project. Their enduring patience, encouragement, and sense of humor have inspired us to see this book through to completion. We thank Erica Judisch and Susan Engelken at Wiley who have patiently monitored our progress and provided gentle nudges and support at every turn. We would also like to thank Peggy Chiappetta, Janessa Price, and Adriana Rodriguez for pulling blocks, organizing histology slides, and conducting literature searches along the way; Deirdre Stuart and Zenya Brown for indexing assistance; Kristine Smith for scanning neglected boxes of kodachromes; Beverly McEwen for endless database searches; Grant Maxie for advice, support, and encouragement; and Josepha DeLay and the AHL Histotechnology team for immunohistochemistry expertise and a willingness to try their antibody magic in new and untested territory. This group has also been endlessly patient with our requests to find blocks, pull slides, prepare recuts, and conduct many special stains.

While many have shared images with us, in particular, our colleagues Hugues Beaufrère and Michael Taylor from the Ontario Veterinary College, Colette Wheler from the University of Saskatchewan, Rick Axelson and Evan Mavromatis at The Links Road Animal and Bird Clinic, Mike Ritter at the New Hamburg Veterinary Clinic, and Markus Luckwaldt of Luckwaldt Mobile Veterinary Services have all provided numerous high quality images for us to use for this book (or found others to supply the images) over the years and we are indebted to these individuals for these visual records. In addition, Dean Percy, John Harkness, Colette Wheler, and Hugues Beaufrère provided valuable comments and edits to the text of the book during its preparation. Many of our current and past colleagues and graduate students at the Animal Health Laboratory and within the Department of Pathobiology, University of Guelph have contributed small mammal necropsy and clinical photographs to the OVC Pathology repository for which we are very grateful.

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1

Rabbits

1.1 Introduction

Domestic rabbits (*Oryctolagus cuniculus*) are descendants of wild European rabbits that were originally found on the Iberian Peninsula by the Phoenicians. Rabbits have been kept by humans for over 3,000 years, largely as a self-replicating source of food, but also for their pelts and later, as pets. Roman writings describe leporaria, walled yards, to keep rabbits contained for hunting. Rabbits were later kept in warrens, courtyards, and islands for breeding and food production, and breeding pairs were released on various islands and in newly discovered lands by naval circumnavigators to ensure a source of fresh meat was available on subsequent visits. In approximately 600 CE, a papal decree declared that unhaired newborn rabbits (laurices) were not meat but instead aquatic species and could be consumed during Lent, leading to a surge of rabbit breeding and domestication in monasteries throughout the Middle Ages. Selective breeding in monasteries gave rise to many of the coat color variants and breeds in existence today. Rabbit breeding for hunting and meat production was initially controlled by seigneurial privilege but with the rise of the middle classes in Europe, raising rabbits became very popular and increasing numbers of animals were kept as pets. Intensification of rabbit farming occurred in parts of Europe and Asia in the early part of the twentieth century, and later, in the early 1950s, in North America. Rabbit breeder associations and specialty hobbyist clubs have been in existence in Europe and North America for over 100 years. Rabbits make gentle and inquisitive pets and are popular with children and adults alike.

When considering rabbit disease, it is important to know the age of the animal and the typical life cycle, be it commercial or pet. The natural lifespan will vary depending upon the size of the rabbit, with larger breeds, such as Flemish giant and New Zealand white rabbits living between 7 and 9 years, while dwarf breeds will live longer; 10–14 years. Rabbits bred for commercial meat purposes in North America tend to be of New Zealand white or Californian background, both of which produce large, fast-growing animals with a high muscle to bone ratio. The white pelts harvested from these animals are used as a by-product for fur trim and felt production. Various spotted and colored hybrid animals may be seen on different farms; however, and other breeds are sporadically introduced from Europe to improve disease resistance and to provide hybrid vigor. In North America, breeding does and bucks kept in commercial meat operations are culled at 2–3 years of age (earlier in Europe) and young rabbits (fryers) are sent to market between 8–14 weeks of age, depending on the efficiency of the operation. Artificial insemination is used in some commercial operations to better manage disease, reproductive cycles, and parturition (i.e., "all in, all out" management systems). Many commercial rabbit breeders also breed or sell rabbits for the pet trade, either dealing directly with pet stores or distributors or by selling animals at the farm gate. While increasing numbers of commercial operations are more selective about barn entry and on-farm biosecurity practices are improving, significant gastrointestinal and respiratory diseases are still present on most of these farms in North America. Many pet rabbits, and there are over 48 breeds recognized by the American Rabbit Breeder Association, come from breeding operations that are not raising animals for meat. These breeding operations may or may not provide routine antimicrobial preventive medications to animals, and the patterns of disease seen in rabbits originating from these sources can be quite different than for commercial meat rabbit operations. Finally, fewer pet rabbits, usually New Zealand white or Dutch-belted breeds, may be adopted directly from research facilities. These rabbits usually originate in commercial laboratory animal breeding facilities and have a very high health status, often being free of gastrointestinal and respiratory infections, which are common in conventionally bred animals. Pet rabbits adopted from rabbit rescue agencies or animal shelters have unknown health backgrounds and may have come from situations of severe neglect. Thus, the types of diseases and conditions that are seen in rabbits will vary considerably, depending on the source.

Pathology of Small Mammal Pets, First Edition. Patricia V. Turner, Marina L. Brash and Dale A. Smith.

Pet rabbits are often neutered at sexual maturity, which occurs between 3–6 months of age, with smaller breeds maturing more rapidly. Neutering is done to manage or prevent behavioral problems as well as to reduce the risk of certain age-related neoplastic conditions. Rabbits coming from research facilities as well as some commercial or show breeding operations may be identified by a tattoo inside one ear. Increasingly, pet rabbits receive micro-chip implants for identification purposes.

Depending on where the rabbit originates, it may be euthanatized by the producer or a veterinary clinic for post-mortem evaluation. Currently accepted on-farm euthanasia practices include blunt force trauma applied to the back of the head, nonpenetrating captive bolt, cervical dislocation, and carbon dioxide inhalation. Animals killed by physical methods may demonstrate oronasal blood staining at post-mortem. Pen mates often cannibalize animals dying on farm and this type of trauma may be recognized by a lack of associated hemorrhage or inflammation. Sedation followed by intravenous or intracardiac barbiturate overdose or anesthetic inhalant gas overdose are more commonly used as euthanasia methods for pet rabbits by veterinary clinics. Because of very rapid tissue deterioration after death, when dealing with investigations of gastrointestinal disease in rabbits coming from commercial operations, it is highly recommended to have the client submit several live affected animals. Post-mortem examination and tissue sampling should occur as rapidly as possible after death.

1.2 Integument Conditions

Rabbit skin is thin and fragile compared with the skin of other species and the pelage consists of a dense undercoat of secondary hairs as well as larger, longer primary guard hairs. Rex rabbits have a defect in the hair growth cycle, resulting in a plush, short, velvety coat lacking the long guard hairs of other breeds. Rabbit hair normally undergoes periods of cyclic and seasonal growth and molting, which may influence hair regrowth patterns following clipping for surgical or other procedures. Regrowth does not occur evenly over the body with independent cycles noted for the dorsum and ventrum. Hair growth cycles also differ among breeds. For example, Angora rabbit hair follicles have been reported to have a growth phase of 14 weeks compared to a 5-week cycle in New Zealand white rabbits, as well as having a higher follicular growth rate. Both these factors likely contribute to the long hairs produced by the Angora breed.

Rabbits have numerous sebaceous glands associated with clusters of hair follicles on their chin (submental gland), feet, and prepuce, which are used for scent-marking (chinning) novel and familiar objects and spaces by sexually mature animals. Modified sebaceous glands are also found in the genital area, and within the rectum. Rabbits are not thought to possess sweat glands but do have modified apocrine glands within the ear (ceruminous apocrine gland), in the perineal area of both sexes, and in the submandibular area. Although mammary glands are not part of the integument, they are discussed in this section because of their cutaneous association.

The external ears of rabbits have only a vertical canal, i.e., they lack a horizontal canal, thus differing from those of other small companion animals, and the vasculature of the ears has an important function in thermoregulation, providing for counter-current heat exchange.

Healthy rabbits are fastidious in their habits and groom their pelage frequently, thus a poor quality, staring hair coat is a sign of poor health. Interestingly, rabbits with orodental disease have a 63 times greater risk of subsequently developing dermatologic disease. This is postulated to be due to decreased nutrition and poor body condition, matting from drooling or other discharge, and decreased grooming in unthrifty or painful animals secondary to chronic dental disease and abscesses.

Skin conditions represent almost 30% of pet rabbit primary care presentations. The most commonly reported conditions include pododermatitis, abscesses, alopecia, parasites, cutaneous masses, and moist dermatitis.

1.2.1 Alopecia

Focal or diffuse alopecia or hair loss is a common presenting condition and there are many potential causes for simple alopecia in rabbits, some of which may be physiologic. Rabbits typically undergo at least two cycles of hair growth and shedding annually and some breeds will undergo four or more cycles. Nutritional and disease status, hormone levels, age, and sex will all influence pelage quality, as well as growth and shedding patterns.

1.2.1.1 Presenting Clinical Signs

Uncomplicated alopecia may present as areas of focal to patchy to generalized hair loss. Owners may report overgrooming, hair pulling or chewing (barbering) or excessive shedding. The skin is intact in these cases unless there are lesions associated with trauma or fighting. Both long guard hairs and secondary hairs may be affected. Alopecia secondary to various endocrinopathies may be associated with vulvar swelling and thinning of the skin in does.

1.2.1.2 Pathology

An infectious etiology should be suspected if hair loss is accompanied by scaliness, pruritus, moist dermatitis or abscessation (see Section 1.2.2 Bacterial Dermatitis). The pattern and distribution of alopecia may provide

clues as to the underlying cause. Hair loss around the muzzle or face may be associated with mechanical abrasion from rough edges on caging or feeders. Similarly, hair loss on the palmar surface of the feet is seen with wire bottom caging (see Section 1.27). Fur chewing can be detected readily on skin biopsy by identification of normal, intact hair follicles and hair shafts that are broken off at the epithelial surface. Simple alopecia related to seasonal, stress-induced or endocrine-related shedding will be detected histologically by complete loss of hair in affected areas with dormant follicles, typically with minimal to no accompanying inflammation and no epithelial scaling or crusting.

Undulating epithelium with disorganized hair follicles and hyperkeratosis has been reported in rabbits with congenital hypotrichosis. Thickening of the skin and ears with crusting, conjunctivitis, and alopecia can be seen in rabbits with severe vitamin B6 deficiency, in conjunction with neurologic signs, such as seizures.

1.2.1.3 Laboratory Diagnostics

Skin biopsies, skin scrapings, microbiologic culture and sensitivity, and circulating steroid hormone and thyroxin levels may be evaluated to differentiate noninfectious from infectious causes of hair loss. It is important to recognize that epithelial thickness will vary markedly depending on the site sampled and control tissues must be sampled from a similar site as affected tissues. Some diagnostic laboratories can determine circulating steroid hormone levels for rabbits, which may be used to support the diagnosis of alopecia-associated endocrinopathy. These levels are not evaluated routinely, however, and appropriate age- and sex-matched reference intervals must be available for comparison. Alopecia has not been reported in association with diabetes mellitus in rabbits.

1.2.1.4 Differential Diagnoses

Normal seasonal shedding and regrowth of the pelage should be differentiated from changes induced by behavioral problems, trauma, adverse stress, inappropriate diet, insufficient dietary fiber content, pregnancy or pseudopregnancy, and mechanical wear from feeders or rough edges on cages. Mechanical abrasion often results in alopecia localized to the nose or face. Behaviorally-induced alopecia is common and may be initiated by boredom (fur chewing), low fiber diets, aggression or other maladjustment syndromes.

Bilaterally symmetrical alopecia in intact does may be associated with hyperestrogenism secondary to ovarian or uterine disease, or other endocrinopathies, including adrenal gland disorders. Pregnant or pseudopregnant does normally will pull hair from their dewlap, forelegs, ventrum, and other parts of their body to line a nest prior to kindling, which may result in thinning of the coat in these places. In pregnant does, the hair loosens up to two weeks prepartum, facilitating nest building. Does exhibiting early to midgestational hair loss and nest-building behaviors are assumed to be pseudopregnant. Hypothyroidism with bilaterally symmetrical alopecia and skin thinning has also been reported in rabbits.

Certain chemotherapeutic medications, such as doxorubicin and adriamycin, as well as radiation therapy, may induce hair loss and clients should be forewarned prior to treatment with these medications or therapies of potential side effects, including alopecia. Sudden psychological or physical stress may also induce focal or generalized hair loss (telogen effluvium). In research settings, strains of autosomal recessive hairless rabbits may be found but congenital hypotrichosis is otherwise rare in pet and commercial meat rabbits. Alopecia has also been reported in rabbits with underlying thymoma (see Section 1.3 Endocrine Conditions).

1.2.1.5 Group or Herd Management

Careful evaluation of housing and husbandry conditions should be implemented for noninfectious causes of alopecia. Dietary adequacy should be ascertained and animal caging should be inspected for surface irregularities if mechanically-induced alopecia is suspected. Co-housed animals may need to be separated to evaluate overgrooming and barbering. Finally, ovariectomy may be recommended in nonbreeding does to prevent pseudopregnancy and associated nest-building behaviors.

1.2.2 Bacterial Dermatitis and Abscesses

Bacterial dermatitis and abscesses may result from local skin or wound contamination or trauma, or systemic distribution of bacteria with secondary skin colonization (Figure 1.1). Abscesses may be single or multiple, and generally contain thick purulent material. Facial abscesses are often associated with dental disease and may fistulate with resulting intraoral or external tracts.

1.2.2.1 Presenting Clinical Signs

All ages, breeds and both sexes may be affected with bacterial dermatitis and abscesses. Affected areas may be erythematous with superficial scaling, induration, alopecia, exudation and ulceration. Cellulitis may develop if subcuticular tissues are involved. In these cases, rabbits may present with pyrexia, anorexia, and depression and may guard the affected area. Moist dermatitis and cellulitis may be malodorous and can become secondarily infested with larvae from *Calliphorid* flies (secondary myiasis, see Section 1.2.4).

The clinical history and distribution of lesions may provide hints as to the etiopathogenesis of the condition.

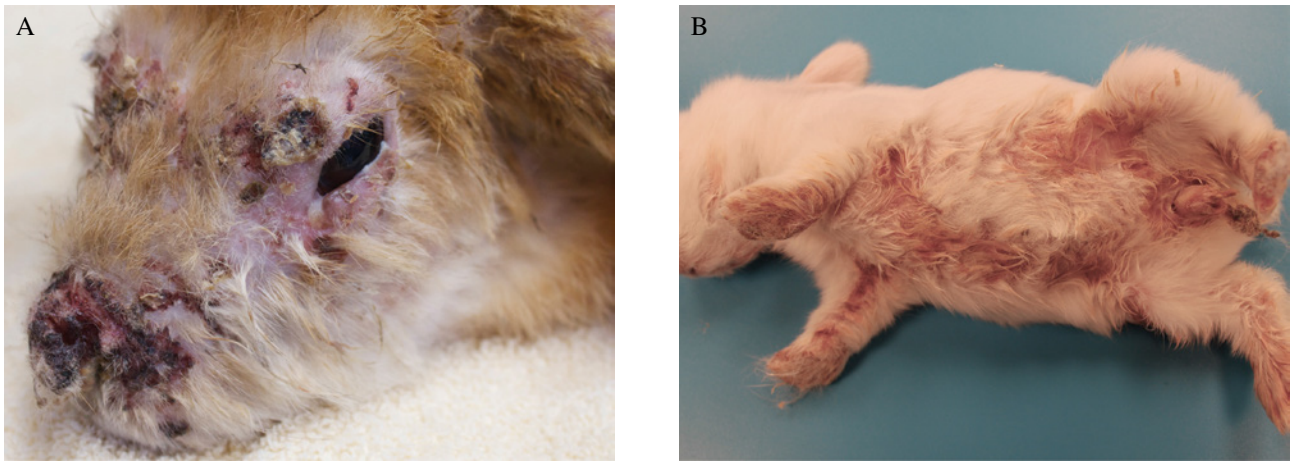

Figure 1.1 A: Fighting wounds in a pet rabbit inflicted by a cagemate, with secondary bacterial infection. B: Staphylococcal pyoderma in a preweaned kit presenting with erythema, patchy hair loss, and exudative dermatitis. Many kits from the same barn were dying with similar skin lesions, which were related to rough nestbox flooring and wet shavings used as nesting material, both of which created dermal microabrasions, predisposing to bacterial infection. *Source:* A: Courtesy of The Links Road Animal and Bird Clinic.

Bacterial dermatitis is usually secondary to other conditions, such as minor trauma, fighting injuries, systemic staphylococcal infections in young kits, abrasions from feeders or caging, poor husbandry with persistent wet or dirty conditions, or urine dribbling or scalding with secondary perineal or ventral abdominal dermatitis and ulceration. Biting and fighting lesions with secondary abscessation are common in pair or group-housed animals, especially if animals are introduced following sexual maturation. Finally, rabbits with impaired mobility or obese animals may be unable to groom effectively, leading to accumulations of urine and feces on the perineal skin with secondary dermal irritation and infection.

1.2.2.2 Pathology

Several well-described bacterial agents and cutaneous disease conditions are recognized in rabbits and are detailed further below. In general, abscesses in rabbits are caused by *Staphylococcus aureus, Pasteurella multocida, Pseudomonas aeruginosa,* or less commonly, by *Proteus* sp., *Bacteroides* sp., and other bacteria. Maxillary and mandibular abscesses arising within the oral cavity may be related to oral or gingival trauma with secondary infection by *Fusobacterium* sp., *Streptococcus* spp., *Actinomyces* sp., or *Arcanobacterium* sp. (Figure 1.2). Rarely, *Francisella tularensis*, the agent of tularemia, will induce cutaneous abscesses in wild cottontail rabbits. Animals infected with this agent usually demonstrate systemic illness and depression, and may die peracutely.

1.2.2.3 Staphylococcosis

The most common agent isolated from lapine abscesses and cases of suppurative dermatitis or cellulitis is *Staphylococcus aureus*, a Gram-positive coccoid bacterium. In addition, *S. aureus* is commonly associated with cases of mastitis (blue breast), pododermatitis (sore hocks), visceral abscessation, metritis, respiratory disease, conjunctivitis, and septicemia in rabbits (see Sections 1.2.5 and 1.2.7). Staphylococcal dermatitis lesions vary with age, sex, and virulence of infecting bacteria. The bacterium is a common opportunistic agent carried on the skin and within the nasal passages and oropharynx of rabbits and their human caregivers.

There are at least five known biotypes of *S. aureus*, based on biochemical properties, and 23 or more phage types, all of which can reassort to create strains of differing virulence, which largely determine the severity of *S. aureus*-induced disease. Low virulence strains induce isolated abscesses and mild dermatitis in rabbits while high virulence strains may induce disease outbreaks with high mortality. Some isolates appear to be host-specific while some are transmissible between species, for example, humans and rabbits. It is not uncommon for animals to be concurrently infected with more than one biotype. In general, rabbit-specific strains of *S. aureus* are susceptible to most antibiotics. However, there have been reports of pet rabbits infected with methicillin-resistant *S. aureus* (MRSA).

Typical superficial lesions caused by *Staphylococcus aureus* include localized, soft to firm nonpainful fluctuant swellings (abscesses) or focal to locally extensive mild to ulcerative exudative dermatitis (Figure 1.2B). Generalized pustular dermatitis with secondary septicemia, internal organ abscessation, and mortality has been noted in young rabbits from affected herds. Multifocal suppurative lesions may be found upon the surface and within the parenchyma of the spleen, liver, kidney, heart,

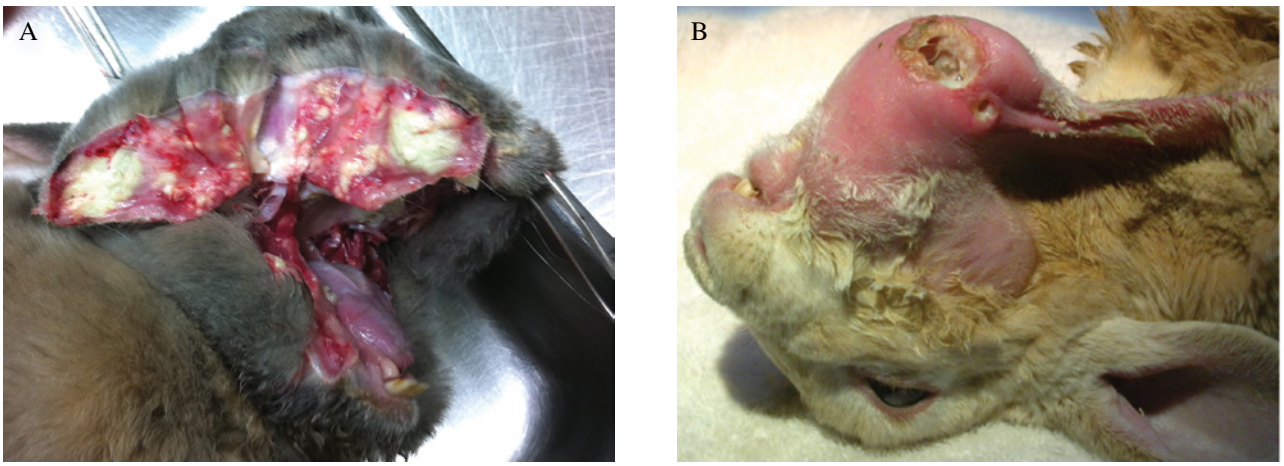

Figure 1.2 A: Multiple facial abscesses in sectioned skin. *Source:* A: Courtesy of M. Luckwaldt. B: Ulcerated submandibular abscess secondary to chronic dental disease. *Source:* B: Courtesy of The Links Road Animal and Bird Clinic.

and lung. Abscesses may be isolated, multifocal, or miliary. Depending on the age of the lesion, marked, predominantly neutrophilic infiltrates may be seen histologically and dense Gram-positive coccoid bacterial colonies are typically abundant around and within lesions, including abscesses. As for other animals, PAS-positive Splendore-Hoeppli material may sometimes be present around dense multifocal aggregates of bacterial colonies (botryomycosis). In peracute cases of staphylococcal septicemia, numerous bacterial colonies may be observed in tissues without significant leukocytic infiltrates or other inflammatory reaction. Death in these cases is presumed to occur from exotoxin-mediated shock. In more chronic lesions with abscessation, a thick fibrous capsule surrounds the necrotic foci, which are comprised of mature and degenerate neutrophils, bacterial colonies, and cellular debris. Edema, granulation tissue, plump fibroblasts, macrophages and multinucleate giant cells may be present in tissues surrounding the abscess.

1.2.2.4 Cutaneous Necrobacillosis

Necrobacillosis (Schmorl's disease) in rabbits is caused by *Fusobacterium necrophorum*, a Gram-negative, anaerobic, non-motile, non-spore-forming, pleomorphic bacterium that is normally found within the gastrointestinal tract and feces of many animals, including rabbits. There are several subspecies of *F. necrophorum*, which may contribute to varying virulence and morphology (e.g., filamentous to rod-shaped). The most significant virulence factors contributing to dermal necrosis and disease are leukotoxin and the lipopolysaccharide found in the bacterial cell wall. Bacterial infection is presumed to occur following fecal contamination of traumatized skin or oral lesions, which may readily occur in a coprophagic animal such as the rabbit. Lesions of mild exudative to deep necrosuppurative dermatitis with induration, erythema, and inflammation may appear around the head, face, neck, and feet. Necrotizing fasciitis, osteomyelitis, septicemia, thromboembolism, and visceral abscessation and necrosis have also been reported in chronic and severe cases.

1.2.2.5 Pseudomoniasis

Pseudomonas aeruginosa is a ubiquitous aerobic, non-spore-forming, Gram-negative, rod-shaped bacterium that causes opportunistic disease in a range of hosts. The bacterium is found in the environment in soil and water and may colonize the skin. Bacterial colonies often have a mucoid phenotype in culture because of prolific bacterial production of surface polysaccharides. These polysaccharides form biofilms that protect the bacteria from common disinfectants, inhibit antibiotic penetration, and in some cases, are linked to genes conferring antibiotic resistance.

In rabbits, *P. aeruginosa* infections may produce moist or ulcerative dermatitis, or cutaneous or visceral abscesses. Moist dermatitis occurs most commonly on the face or forelimbs of animals with malocclusion and secondary ptyalism, and in animals that are maintained in wet housing conditions, or under the dewlap or between cutaneous folds in heavy rabbits. Moist dermatitis is characterized by serous to serosuppurative exudates with erythema, alopecia, and matting of hair around the lesion. Chronic lesions may ulcerate. The purulent debris and hair surrounding these lesions may be malodorous and have a characteristic bluish-green cast, caused by bacterial expression of pyocyanin, an exopigment and virulence factor.

1.2.2.6 Cutaneous Spirochetosis

Treponematosis (venereal spirochetosis, rabbit syphilis, vent disease) is caused by a Gram-negative

spirochete, *Treponema paraluiscuniculi*. The condition is not zoonotic and occurs sporadically in breeding and pet rabbits. The spirochete is transmitted horizontally to kits during suckling and during breeding in adult animals. Lesions develop 3–6 weeks following exposure and are most prominent on the mucocutaneous junctions of the genitalia, perianal skin, nose, mouth, and eyelids. The lesions begin as foci of erythema and edema and progress to papules or vesicles, followed by focal ulceration with crusting, and scaling or hyperkeratosis (Figure 1.3). Histologically, skin lesions may have moderate acanthosis, spongiosis, and orthokeratotic hyperkeratosis, with multifocal areas of erosion and ulceration. Typical argyrophilic long slender spirochetes may be seen within the serocellular crust with a Warthin-Starry stain.

Mild or subclinical disease is most common, but *T. paraluiscuniculi* infection has also been associated with abortion, metritis, and infertility in breeding does. This condition may present with similar cutaneous manifestations as for *Pasteurella multocida* infection (i.e., moist nasal dermatitis, cheilitis, conjunctivitis, and rhinitis). It is an important differential to consider as spirochetosis may be readily treated, whereas chronic pasteurellosis often requires repeated treatment and is rarely cured.

1.2.2.7 Laboratory Diagnostics

Bacterial dermatitis and abscesses are diagnosed via culture and sensitivity of lesions or exudate, cytology and/or skin biopsy. In-toto removal of abscesses is recommended to minimize environmental contamination. Increases in total white blood cell counts may not be seen with severe bacterial infections in rabbits; however, marked increases in relative neutrophil (heterophil) numbers may be noted. Most laboratories do not routinely

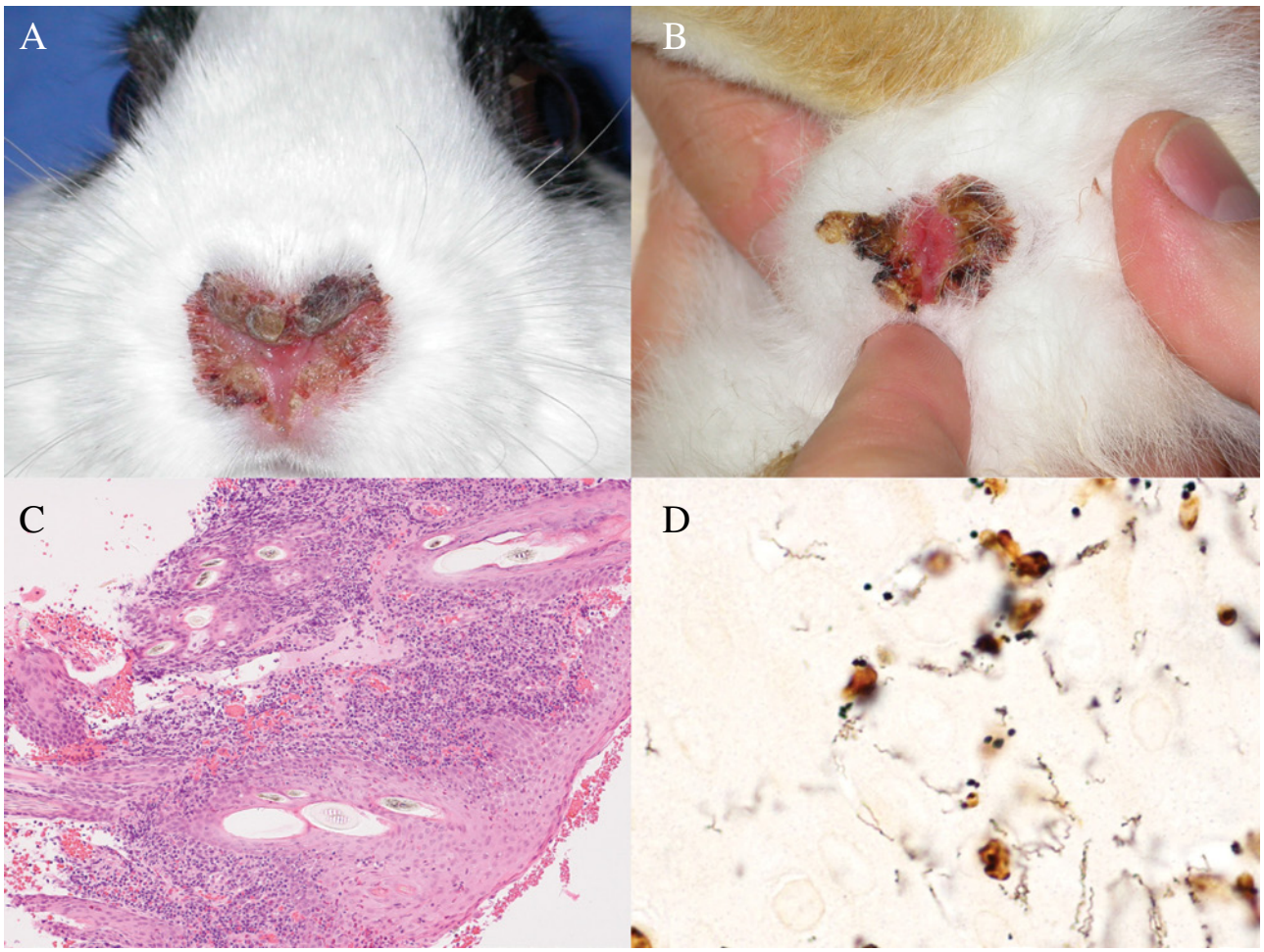

Figure 1.3 A: Focal ulceration and crusting of the nasal skin in a rabbit with cutaneous treponematosis. B: Venereal lesions on the same animal. C: Infection with *Treponema paraluiscuniculi* results in focal erosion with acanthosis, crusting, and moderate mixed, predominantly neutrophilic infiltrates. D: A Warthin-Starry stain demonstrates long, slender *T. cuniculi* spirochetes. *Source:* A and B: Courtesy of The Links Road Animal and Bird Clinic.

conduct phage typing for *S. aureus*, however, phage typing may be necessary to determine root causes of disease outbreaks.

The appearance and distribution of gross lesions of rabbit syphilis are often diagnostic. Diagnosis of *Treponema* sp. in formalin-fixed tissue sections requires Warthin-Starry silver staining to visualize the spirochetes, which may be few in number. Dark field microscopy of fresh scrapings of lesions and serological tests, including a hemagglutination test, fluorescent *Treponema* antigen preparation (FTA) and the Rapid Plasma Reagin (RPR) test, may be employed to aid in the diagnosis of this disease. However, anti-*Treponema* antibodies are slow to develop, requiring 5–6 weeks from the time lesions appear, suggesting that serology is less effective for diagnosing active cases.

1.2.2.8 Differential Diagnoses

Other possible causes of dermatitis include dermatophytosis, ectoparasitism, and contact allergy. Differential diagnoses for abscesses include cutaneous cysts, lipomas, cuterebriasis, hematoma, or neoplasia, such as lymphosarcoma. *Yersinia pestis* infection with cutaneous swellings ("bubos") occurs rarely in wild cottontail rabbits in the United States and may be transmitted to humans during handling of sick animals or carcass dressing.

1.2.2.9 Group or Herd Management

Staphylococcosis is a major cause of carcass condemnation at abattoirs, and induces significant morbidity, culling, and mortality in enzootically infected commercial rabbit meat operations due to visceral and cutaneous abscesses, and reproductive failure. Herd infection rates of up to 70% have been reported. In these situations, eradication via test and cull procedures and repopulation with clean animals is the only proven method of eliminating the agent from a herd. Interspecies transmission of *S. aureus* may occur, and appropriate hand-washing procedures should be in place after handling animals with suspect lesions.

Rabbit spirochetosis tends to be self-limiting, with spontaneous regression of lesions usually occurring within several weeks. Untreated rabbits can remain seropositive, suggesting a carrier state, possibly due to maintenance of the organism in regional lymph nodes. For these reasons, treatment of affected rabbits and other in-contact rabbits is the preferred method of control.

1.2.3 Dermatophytosis

Dermatophytosis (ringworm) is a superficial fungal infection of keratinized structures such as the hair, skin, and nails, and is a common clinical and subclinical entity in pet and commercial production rabbits. Disease is typically mild; however, the chronic treatment required for eradication, potential for cross-species transmission, including to humans, and persistence of spores in the environment makes this an agent of concern whenever it is diagnosed. *Trichophyton mentagrophytes* is the organism isolated most commonly from rabbits; however, *Microsporum* spp. may also infect rabbits. Young age, suboptimal housing environments, poor nutrition, and intercurrent disease may predispose animals to clinical disease. A carrier state is common in otherwise healthy rabbits with a reported prevalence rate of 4–36%.

Other types of deep or systemic mycoses or yeast infections in rabbits are rare. *Malassezia cuniculi* is a newly identified yeast cultured from the ear canal and inguinal areas of otherwise healthy rabbits but the organism has not been associated with clinical disease in the absence of predisposing factors, such as immunocompromise.

1.2.3.1 Presenting Clinical Signs

Typical presenting signs of dermatophytosis include nonpruritic or mildly pruritic, focal to patchy alopecia with erythema, and scaling of skin around the margins of the lesion. Surrounding hair shafts may be broken, with a stubbled appearance. Lesions are usually present on the face, extremities, and nail beds although they can be found anywhere on the body.

1.2.3.2 Pathology

Histologically, there is hyperkeratosis, epidermal and follicular acanthosis with mild neutrophilic to pyogranulomatous perivascular and intraepithelial dermatitis and folliculitis of affected skin. Arthroconidia and septate fungal hyphae are present in skin sections and may be visualized better following periodic acid-Schiff or Gomori's methenamine silver staining of sections.

1.2.3.3 Laboratory Diagnostics

Definitive diagnosis of dermatophytosis may be made from fungal culture of skin scrapings and debris, growth in Dermatophyte Medium (DTM), and microscopic evaluation of skin biopsies. Species-specific identification of the infecting organism requires culture and, possibly, molecular diagnostic methods.

1.2.3.4 Differential Diagnoses

Barbering or overgrooming, mechanical trauma, contact allergies, and external parasitism are potential differential diagnoses for dermatophytosis.

1.2.3.5 Group or Herd Management

Transmission of arthroconidia occurs by direct contact and via fomites. Infections are readily transmitted between animals that live in close proximity or that are

housed indoors at high densities. Because infectious material may remain viable in the environment for several years, environmental sanitation is as important as individual animal treatment for managing this disease. Dermatophyte infections are potentially zoonotic and may be spread to humans and other animals in the household or on premises. Appropriate hand-washing regimes should be in place after handling animals. Young, pregnant, or immunosuppressed animals or humans may be at increased risk of contracting the disease.

1.2.4 External Parasites

There are a number of important ectoparasitic infestations of rabbits, including fur and ear mites, fleas, lice, and myiasis, which may induce pruritus, alopecia, and dermatitis. Infestations with ectoparasites are usually readily identified during careful gross examination of the pelage and microscopic evaluation of skin biopsies may not be necessary. Presenting signs, pathology, and other diagnostic information for the most important external parasites of rabbits are detailed below.

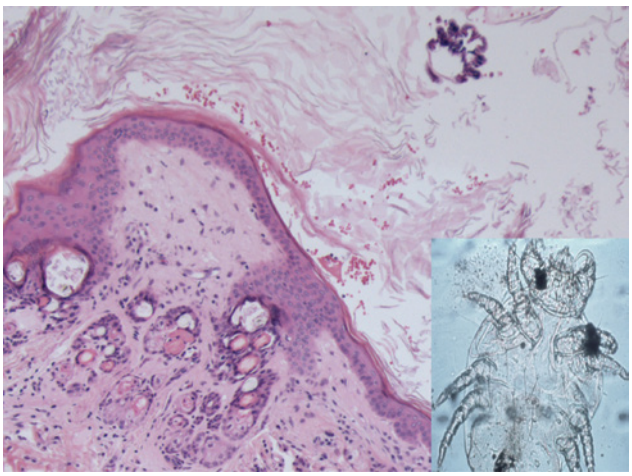

Figure 1.4 Dermatitis in a rabbit caused by *Cheyletiella parasitovorax*. Significant scaling dermatitis is present and there is minimal dermal inflammation. An adult mite can be seen in the superficial scale. Inset: Wet mount of *C. parasitovorax* mite. *Source:* Courtesy of C. Wheler.

1.2.4.1 Fur Mites

Fur mites are common in wild, pet, and commercial rabbits, and *Cheyletiella parasitovorax* ("walking dandruff") is isolated most frequently. It is a nonburrowing, actively moving mite with a broad host range, including humans, that lives on superficial debris and lymph secretions obtained by piercing the skin with chelicerae (paired piercing mouthparts). All life forms (i.e., larvae, nymph and adult) may be found on the host; however, the adult female mite may survive off the host for a week or longer. Presenting signs may include mild pruritus, flaking, scaling skin, seborrhea, and alopecia anywhere on the body, although many animals will be asymptomatic. Mites are pale yellowish-white, up to 0.54 mm long, and can be visualized moving around at the base of hair shafts with the unaided eye when the hair coat is parted (Figure 1.4). Diagnosis of an infestation is achieved best by direct observation or microscopic evaluation of a cellophane tape impression of the pelage. Characteristic morphologic features of adults include four pairs of legs each with a distal comb, instead of a claw. Histologic examination of skin biopsies may be nondiagnostic, and may show only orthokeratotic hyperkeratosis and mild acanthosis with superficial perivascular dermatitis.

Leporacarus gibbus (*Listrophorus gibbus*) is another common non-burrowing fur mite of wild and domestic rabbits that can be found on the dorsal flank, extremities, or almost anywhere on the pelage. It spends its entire life cycle on the host. Although widely considered to be nonpathogenic, the mite may induce mild pruritus, scaling, moist dermatitis, and alopecia in infested animals and may be diagnosed via methods as described above. It is readily seen, with the unaided eye or with a hand lens, as 0.2–0.5 mm long brown specks attached to the hair shaft. The mite is motile, brown, and laterally compressed with four pairs of legs and a projection from the head over the mouth parts. *L. gibbus* has specially adapted legs that allow it to cling to hair shafts. Human infestations resulting in erythematous and pruritic, papular dermatitis have also been reported.

1.2.4.2 Ear Mites

Otitis externa secondary to ear mite infestations is common in pet and meat-producing rabbits and is caused by *Psoroptes cuniculi*, a large, white, ovoid, highly motile, non-burrowing mite that is up to 0.7 mm long. *Psoroptes* sp. feed on lymph and cellular debris and pierce the skin with their mouthparts. Both mechanical trauma and hypersensitivity to mite feces are thought to induce irritation and inflammation. Early infestations may be inapparent, although experimental studies of acute and chronic *Psoroptes* infestations in rabbits have demonstrated decreased activity levels, chinning, and other abnormal behaviors. Heavy infestations lead to head shaking, ear drooping, intense pruritus with secondary excoriations, hyperemia, induration, serous exudation, and ulceration along with decreased food intake and body weight losses. A dense gray-brown serocellular crust may be visible within the ear canal (Figure 1.5). *Psoroptes* sp. are seen readily in scrapings of ear canal debris collected in mineral oil. Mite species should be verified to rule out sarcoptic and notoedric

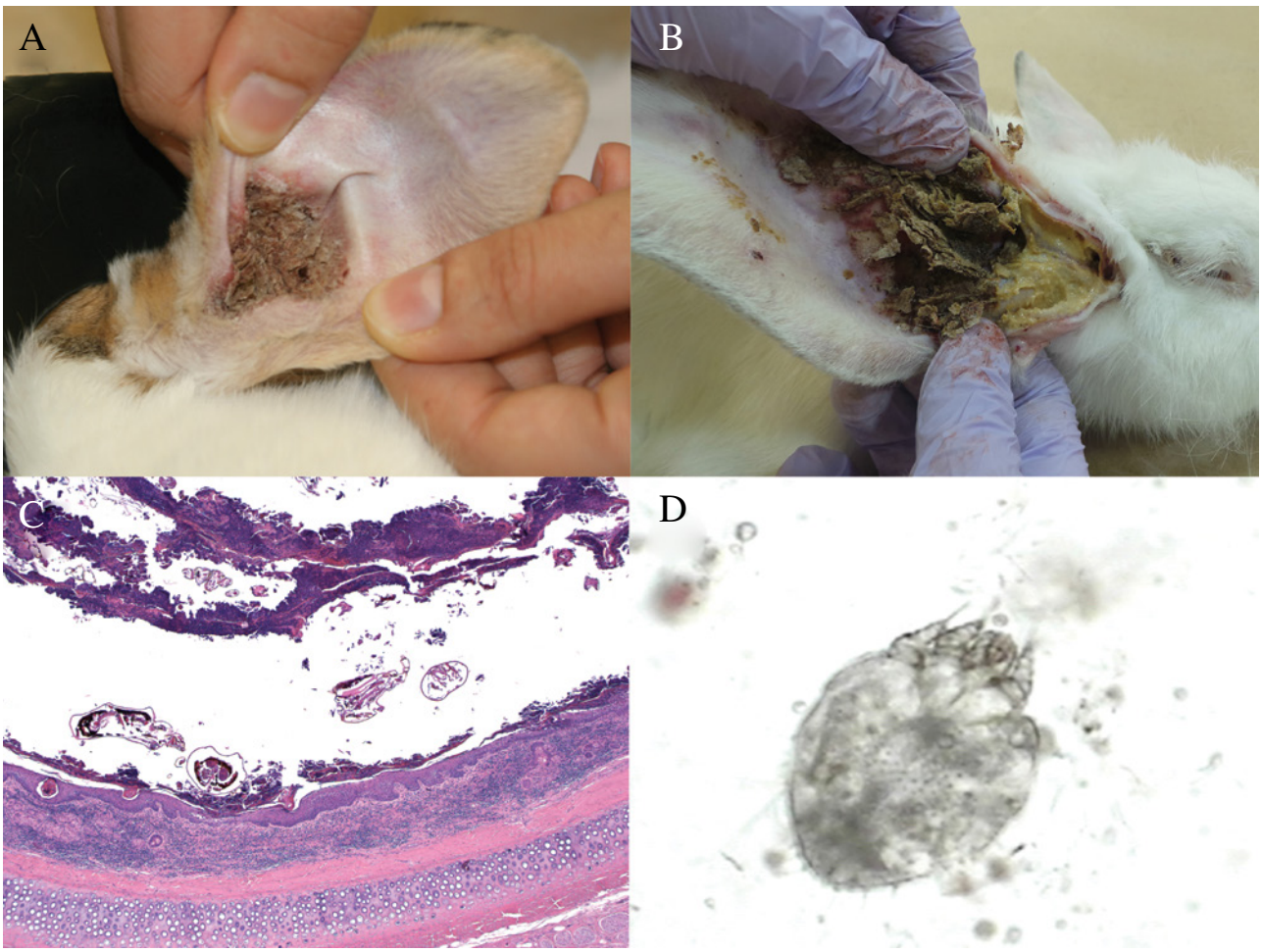

Figure 1.5 A: Mild ear mite infestation in a pet rabbit. B: Severe infestations with *Psorpoptes cuniculi* can lead to intense pruritus with excoriations and secondary bacterial infections, as in this rabbit with secondary dermatitis. C: Mites are readily noted feeding on the surface of the ear canal in microscopic section. D: A *Psoroptes cuniculi* mite from an ear swab. *Source:* A: Courtesy of The Links Road Animal and Bird Clinic.

mange, which may have more serious implications. Ectopic psoroptic dermatitis of the face and ventrum has been reported. Lesions include the appearance of thick serocellular crusts with erythematous borders, exudative dermatitis with matted hair, and accompanying alopecia.

Environmental treatment is critical with this agent as female mites can live off the host for several weeks, leading to re-infestation. *Psoroptes cuniculi* has a scrupulous host range and is not zoonotic.

1.2.4.3 Other Mites

Sarcoptic (*Sarcoptes scabiei var. cuniculi*) and notoedric (*Notoedres cati*) mange are uncommon in pet and commercial rabbits. Both of these burrowing arthropods are round with short stubby legs that do not project beyond the body margins, and blunt mouth parts. They are seen in less well-haired areas of the skin, including the face, legs, and ear canal, and induce an intense pruritus with marked inflammation, exudation, ulceration, secondary pyoderma, and anorexia. They can be detected only with deep skin scrapings or skin biopsy. Histologic features include parakeratotic hyperkeratosis and acanthosis, with epidermal neutrophilic infiltrates. Cross-sections of mites are present within the stratum corneum and demonstrate a thick chitinous cuticle with short appendages, skeletal muscle and a body cavity with gastrointestinal and reproductive tracts. Both mite species may infest human handlers.

Demodex cuniculi is rarely reported as a cause of clinical signs in rabbits, presenting as mild pruritus, seborrhea and focal to patchy alopecia. Mites have a typical narrow, elongated appearance and are present in the hair follicles, as per other *Demodex* spp. Whereas the prevalence of infestation is unknown, the pathologic significance is thought to be minor.

1.2.4.4 Cutaneous Myiasis

Both primary and secondary myiasis (fly strike) may occur in rabbits. Primary myiasis occurs when larvae penetrate living tissue to feed and develop (obligate host life cycle), whereas secondary myiasis occurs when flies that feed and develop on decomposing organic matter lay eggs on soiled or necrotic tissue of animals, with subsequent larval development (opportunistic host life cycle). Primary myiasis occurs in rabbits of all ages and health status, whereas secondary myiasis typically is seen in neglected or debilitated animals with open sores, moist dermatitis, or fecal or urine soiling of the hind end.

In North America, primary myiasis in rabbits is caused by botfly larvae (*Cuterebra* spp.) and wild and domestic species are susceptible. Human botfly (*Dermatobia hominis*) infestation of rabbits is seen in neotropical areas where this parasite is endemic. Rabbits that are housed or exercised outdoors are more likely to be infested with *Cuterebra* spp. larvae, and most infestations occur at hot, humid times of the year. Flies lay eggs on the tips of grasses at the entrance to the burrow or near the nest or cage. After hatching, larvae attach to the pelage of a passing host and are subsequently ingested during normal grooming. Most larvae migrate through the body to subcutaneous sites for further development, but they may also migrate to aberrant locations anywhere in the body. Presenting signs will depend on the migration site and number of larvae, but lesions generally appear as large, nonpainful fistulous swellings, approximately 1–3 cm diameter on the neck, dorsum, axillary, or inguinal areas (Figure 1.6). Each swelling contains a single larva and upon close examination, a breathing pore is present in the surface of the swelling. Larvae are white, cream or black with prominent spines over their body surface.

Figure 1.6 *Cuterebra* spp. larva being removed from the head of a rabbit. *Source:* Courtesy of The Links Road Animal and Bird Clinic.

A serosuppurative discharge may be present around the breathing pore with matting of the surrounding hair. Young rabbits with heavy infestations may become debilitated and anorexic, and death of a larva can lead to rapid shock and death of the host. Surgical removal of the larvae is curative. Left untreated, larvae will complete development in 1–2 months and emerge spontaneously from the cyst to pupate. Aberrant migration of larvae has been reported in the brains of pet rabbits housed outdoors during warm weather, with subsequent death. Larval migration tracts in the brain and spinal cord of these animals contained localized areas of malacia, necrosis, and hemorrhage with moderate mixed leukocytic infiltrates.

Secondary myiasis occurs when species of *Calliphorid* flies (blow flies) are attracted to oviposit on feces- or urine-stained matted hair or open, untreated wounds or areas of exudative dermatitis. Affected animals may be debilitated, obese, or suffer from diarrhea, neglect, or other conditions that hamper normal grooming, including malocclusion. Animals housed indoors or outdoors may be infested and warm, humid environments promote fly and larval development. Larvae (maggots) hatch within 24 hours or less and feed on superficial debris and necrotic tissue, contributing to a fetid odor. Larvae are visible grossly once matted hair and necrotic tissue are removed and debrided. Secondary bacterial infection of the necrotic, infested areas may occur and animals may die of shock or sepsis, regardless of treatment.

1.2.4.5 Fleas

Flea species infesting rabbits include *Cediopsylla simplex* and *Spilospyllus cuniculi*. In households with dogs or cats, indoor pet rabbits are more likely to be infested with *Ctenocephalides canis* or *C. felis*. Fleas and their feces (flea dirt) may be found on the face, ears, or within the pelage, particularly over the dorsal trunk, and animals may present with pruritus, alopecia, focal erythema, and scaling at the flea bite sites. Hypersensitivity to flea saliva has been reported in rabbits. Environmental decontamination and treatment of other susceptible household pets are important for eradication. In geographical areas where the diseases are prevalent, fleas can serve as a vector for myxomatosis, tularemia, and plague.

1.2.4.6 Lice

Haemodipsus ventricosus, the rabbit louse, is a sucking louse that affects domestic and wild rabbits, and wild hares. Infestation of pet and commercial rabbits is rare and associated with neglect or conditions of poor husbandry. The dorsal trunk is affected more commonly and presenting signs may include pruritus, alopecia, erythematous papules, anemia, weakness, and, if infestations

are heavy, death. Lice are up to 2.5 mm in length and can be seen by the unaided eye. A diagnosis of pediculosis is usually possible following careful gross examination of the pelage. Lice will migrate away from the skin when the pelt is cooled and can be detected post-mortem on the tips of hairs after chilling the carcass for 30 minutes in a plastic bag. The eggs are large and ovoid and are cemented to the base of the hairs and are readily apparent. Transmission is by direct contact between animals or with contaminated bedding. As with fleas, lice can serve as a vector for myxomatosis, tularemia, and plague.

1.2.4.7 Ticks

Several species of ticks can parasitize pet and commercial rabbits. The rabbit tick, *Haemaphysalis leporispalustris*, is common in wild rabbits and may harbor various zoonotic bacteria and spirochetes, including *Borrelia burgdorferi*, as well as *Francisella tularensis*. Rabbit ticks rarely bite humans or other mammals. Severe infestations may lead to marked anemia and weakness.

1.2.4.8 Laboratory Diagnostics

In most instances, diagnosis of external parasitism is obvious in live animals or on gross examination of the carcass. Definitive diagnosis of sarcoptic, notoedric, or demodectic mange requires skin biopsy or deep skin scrapings. Speciation of mites, in particular, is important, as some are zoonotic or may infest other household pets.

1.2.4.8 Group or Herd Management

Quarantine of new arrivals should occur for at least two weeks before introducing new rabbits into a herd or household with other rabbits to minimize transmission of ectoparasites or other diseases to naive animals. Individual treatment of pet animals may be possible for mite and flea infestations. However, treatment and subsequent eradication of fur or ear mites from large breeding herds are difficult. Meat withdrawal times must be specified for any therapeutics given to meat-producing rabbits, and caution should be exercised when extrapolating ectoparasite treatments from other species. Organophosphate toxicity has been reported in rabbits associated with malathion dipping for mites. Environmental decontamination is important for all external parasites to minimize re-infestation of rabbits or other species. Owners should be educated regarding protecting pet rabbits from parasite transmission when rabbits are housed or exercised outside, and informed about potentially zoonotic diseases, including rabbit ectoparasites and diseases that they may transmit. Owners should be advised to seek medical attention if they experience any consistent signs of disease such as pruritus. Cases of suspect animal neglect, characterized by severe, untreated ectoparasitism, may require further investigation by local anti-cruelty agencies.

1.2.5 Mastitis

In commercial rabbit herds, mastitis (blue breast) is a significant cause of economic loss and suffering, and culling of breeding does, and may occur at any time during lactation. The common name for this condition arises from the cyanosis and necrosis seen in affected glands. Mastitis may occur also in pet or commercial pseudopregnant does.

1.2.5.1 Presenting Clinical Signs

Does with mastitis may present with one or more indurated, erythematous mammary glands that are painful. Animals may be depressed, lethargic, and pyrexic, and some animals will die acutely. Agalactia can occur and does may refuse to nurse kits, both factors resulting in subsequent kit mortality. Recrudescence of mastitis may occur in later lactations in does that recover and are rebred.

1.2.5.2 Pathology

Both acute gangrenous mastitis and chronic suppurative mastitis with secondary abscessation may occur, the differences in presentation likely attributable to bacterial virulence factors and host immunity. *Staphylococcus aureus* is isolated in the vast majority of cases, and *Pasteurella multocida* and *Streptococcus* spp. are less common. Enterotoxin from high virulence strains of *S. aureus* may induce immunosuppression in the host. Both the bacterial biotype and presence of various phages contribute to bacterial virulence.

The acute gangrenous form of mastitis is less common and gross signs include hemorrhage, edema, and cyanosis of the affected glands. In the more chronic form, glands are firm, with edema, necrosis, and purulent exudate noted on cut section. Teats overlying affected glands may become swollen and cyanotic, and a purulent to brown discharge may be present. Subcutaneous abscesses, pododermatitis, and pyometra also may be present in affected animals. The etiopathogenesis of the condition is unknown and may occur through trauma to the teats or glands, autoinoculation during grooming, or from kits, as kits from infected does have been demonstrated to infect naive does during suckling.

Histologically, there are marked neutrophilic infiltrates within the stroma of the affected gland, with lesser numbers of lymphocytes, plasma cells, and macrophages. Edema, hemorrhage, and necrosis may be present. Discrete abscesses and dense colonies of Gram-positive cocci are generally present in the affected areas. There may be full thickness necrosis of the overlying skin.

1.2.5.3 Laboratory Diagnostics

Bacterial cultures of draining fluid or biopsied or post mortem tissue should be conducted to confirm the

infectious agent. Cultures may be sterile, however, suggesting that exotoxins may be important in disease pathogenesis. Bacterial biotype and phage typing are not routinely performed on submitted samples and should be specifically requested, if needed.

1.2.5.4 Differential Diagnoses

Cutaneous myiasis, subcutaneous abscesses, and benign and malignant tumors should be considered as potential differential diagnoses in mature does with ventral cutaneous swellings.

1.2.5.5 Group or Herd Management

Because of the significant impact on overall operation, commercial breeding does with mastitis should be culled to minimize bacterial burden in the environment. Cages should be examined for rough edges or points, which may induce trauma. New entries into the herd should be quarantined for at least two weeks to minimize spread of infectious agents to naive animals. There is currently no vaccine available to prevent staphylococcosis in rabbits.

1.2.6 Cutaneous Masses and Neoplasia

While commercial laboratory and meat rabbits are usually relatively short-lived, various cutaneous masses are seen with increasing frequency in aged pet animals. Some tumors are virally mediated, and it is helpful for prognosis to classify masses based on malignant behavior and viral induction. Non-viral, benign neoplastic masses seen with regularity in rabbits include collagen hamartoma (sometimes reported as dermal fibrosis), collagenous nevus, cutaneous xanthoma, trichoblastoma, trichoepithelioma, fibroma, lipoma, and nonviral papilloma. Other cutaneous masses that are not virus-associated include squamous cell carcinomas (Figure 1.7A), basal cell tumors (Figure 1.7B), piloleiomyomas and piloleiomyosarcomas (Figure 1.8), keratoacanthomas, soft tissue sarcomas (Figure 1.9), fibrosarcomas, cutaneous lymphomas, and malignant melanomas. Melanomas are highly uncommon in pet rabbits, although both amelanotic and pigmented forms have been described. Viral-mediated non-malignant masses and lesions include Shope fibroma, cottontail rabbit papilloma, oral papillomatosis, leporid herpesvirus-4-induced lesions (LeHV-4; see Respiratory-LeHV4), and myxomatosis.

Invasive and recurrent post-vaccinal interscapular fibrosarcoma has been reported in a pet rabbit in Europe following vaccination with commercial products for myxoma virus and rabbit hemorrhagic disease virus. Tumor characteristics included marked proliferation of pleomorphic neoplastic fibroblasts amidst a background of multinucleated giant cells and infiltrating lymphocytes.

Various cutaneous glandular tumors are seen on occasion, including Meibomian gland adenoma, submandibular apocrine gland hyperplasia, adenoma and adenocarcinoma, mammary gland adenocarcinoma, and sebaceous adenocarcinoma of the external auditory ear canal. Some authors have reported rare cases of mesenchymal tumors in rabbits with cutaneous manifestations, such as myxosarcoma, giant cell sarcoma, eosinophil granulocytic sarcoma, osteosarcoma, leiomyosarcoma, or rhabdomyosarcoma (Figure 1.10), but these are uncommon. Stromal myxoid differentiation is reported frequently with anaplastic sarcomas and this has been

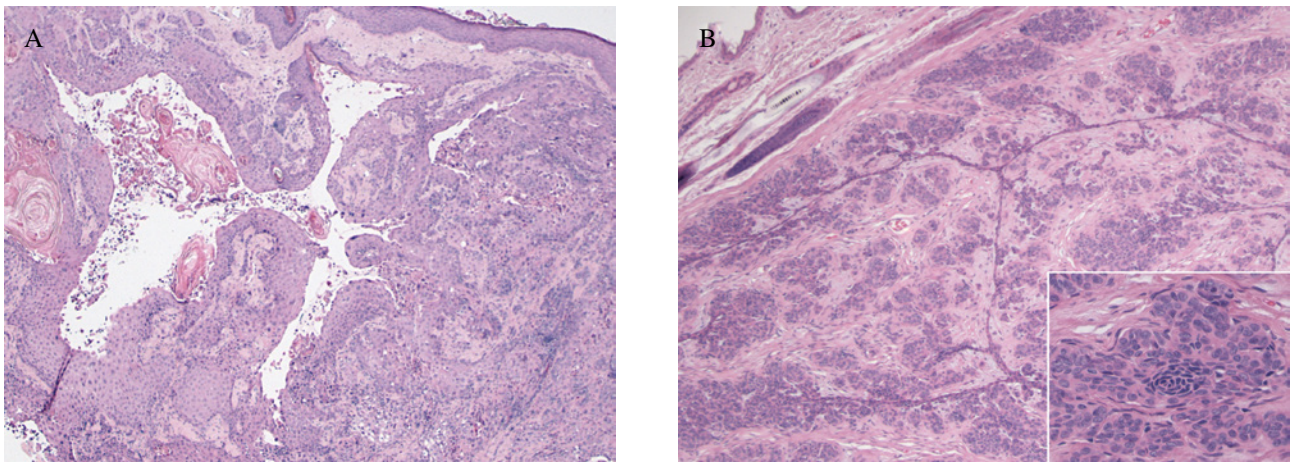

Figure 1.7 A: Invasive squamous cell carcinoma with disordered epithelial maturation and formation of keratin pearls in the pinna of a rabbit. B: A well-differentiated basal cell tumor from the neck of a rabbit. Inset: The tumor is moderately cellular, well-demarcated, multilobular, unencapsulated, and composed of basilar cells arranged in variably sized islands, separated by a moderately dense fibrous stroma.

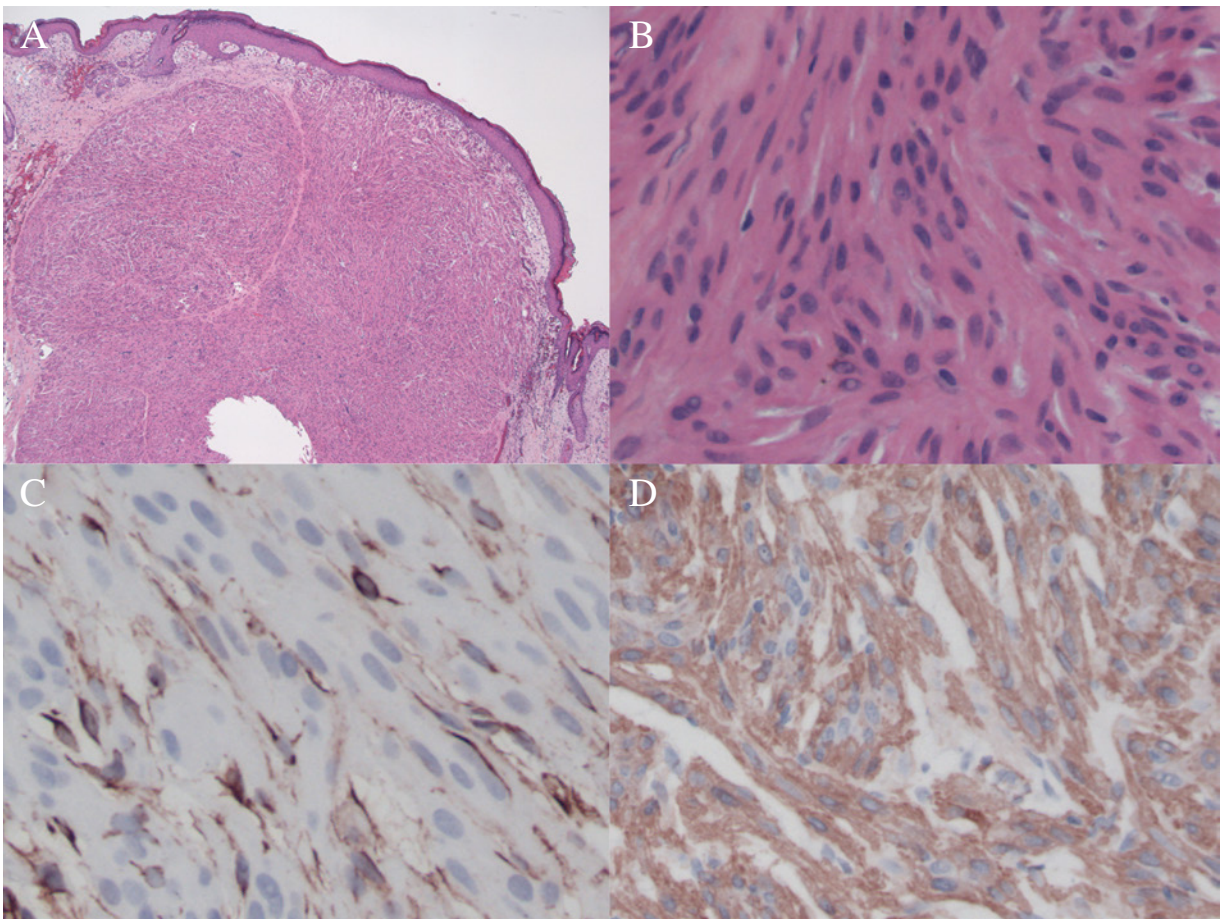

Figure 1.8 A: Cutaneous mass from a 9-year-old neutered female rabbit. The mass is round, raised, and circumscribed but not encapsulated, and composed of plump eosinophilic interweaving spindle to strap-like cells resembling smooth muscle cells. B: The strap-like tumor cells resemble the arrector pili muscles associated with the nearby hair follicles. Nuclei within these strap-like cells are round to ovoid to rectangular with mild anisokaryosis and no mitotic figures are seen. C: Tumor cells are positively labelled for vimentin. D: Tumor cells have strongly positive cytoplasmic labeling for smooth muscle actin, consistent with a diagnosis of piloleiomyoma.

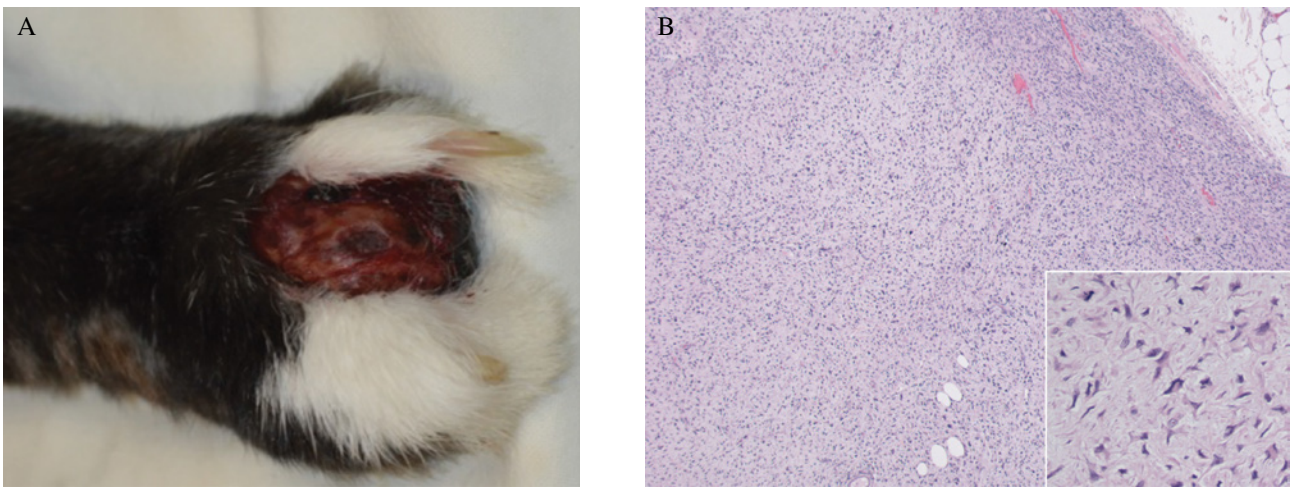

Figure 1.9 A: An invasive soft tissue sarcoma of the foot of a rabbit. B: Tissue from a large, lobulated scapular mass in a 9 year-old male rabbit. Smaller nodules were present in the lung and aorta. The mass is composed of a monotypic population of spindle cells within an abundant fibrovascular stroma. Inset: The cells have indistinct cellular borders, abundant eosinophilic fibrillar cytoplasm, convoluted angular nuclei, and there is 4-fold anisocytosis and anisokaryosis, with rare mitoses. A poorly differentiated sarcoma was diagnosed. *Source:* A: Courtesy of The Links Road Animal and Bird Clinic.

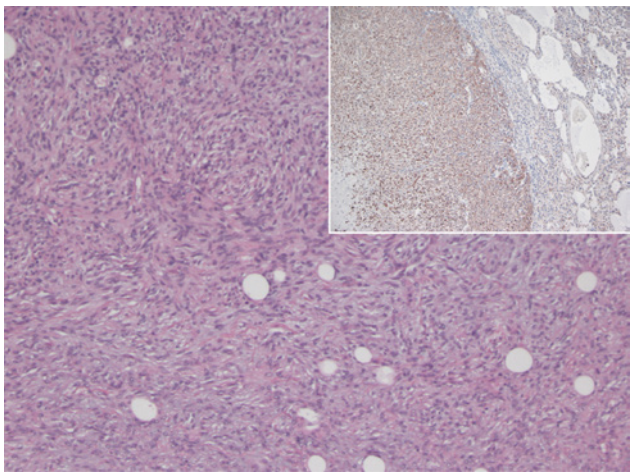

Figure 1.10 Rhabdomyosarcoma of the heart, skin (depicted) and lung (inset). Multiple variably-sized nodules of spindle cells forming whorls and clusters are seen within the dermis. The neoplastic cells have variably-sized nuclei, a strap-like appearance, and up to 5 mitoses/400x field. Immunohistochemistry of the tumor demonstrated positive cytoplasmic labeling for vimentin (inset: lung mass, counterstain: Mayer's hematoxylin) and muscle actin, but the tumor was negative for S100 and smooth muscle actin.

suggested as a rabbit-specific phenotypic characteristic. All tumor types have similar characteristics to those seen in other companion animal species and the long-term prognosis is based on adequacy of resection of tumor margins, cellular atypia, necrosis, pleiomorphism, mitoses, and metastases. Masses that are more common or that are specific to rabbits are discussed in greater detail below.

1.2.6.1 Laboratory Diagnostics

Fine needle aspirates and surgical or excisional biopsies are highly recommended when cutaneous masses are noted in rabbits to differentiate between infectious and neoplastic diseases. Additional testing may be required to confirm suspected viral infections, including serology, virus isolation, electron microscopy, and immunohistochemistry.

1.2.6.2 Collagen Hamartoma

Collagenous hamartoma (collagen nevus) is a very common nonneoplastic proliferative lesion seen in most breeds and both sexes of rabbits. Usually, masses are noted by the owner on the ventral abdomen or dorsum and present as nonpainful firm discrete masses or plaques, sometimes with sparse overlying hair or alopecia (Figure 1.11). Histologically, they are bland in appearance, consisting of localized dense collagen aggregates and scattered fibroblasts within the dermis with no evidence of dermal inflammation. The overlying epithelium and adnexal structures may be mildly attenuated and atrophic.

1.2.6.3 Trichoblastoma

Trichoblastoma is one of the most common tumor types seen in rabbits and these tumors are usually benign and slow-growing. Solitary masses may be found anywhere on the body, and are seen equally in males and females. Historically, many of these masses were identified as basal cell tumors; however, because of morphologic similarities to tumors seen in dogs and cats, they are identified more correctly as trichoblastomas. The tumor is thought to derive from primitive follicular cells within the dermis and there are several subclassifications, based

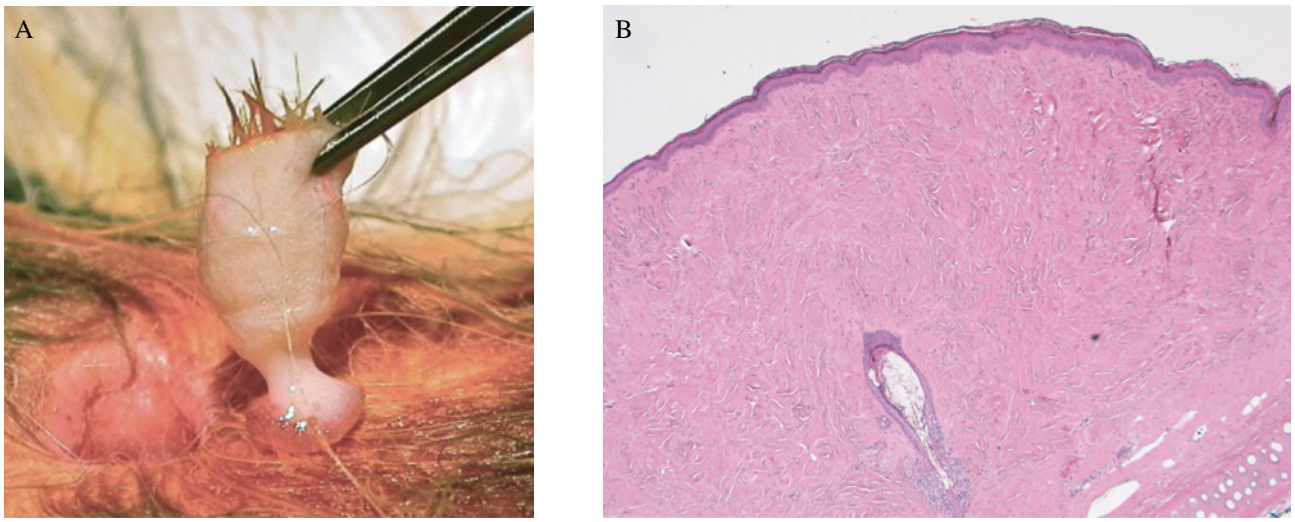

Figure 1.11 Collagen hamartoma in skin biopsy. A: Firm, plaque-like mass was present in the skin of the rabbit. Microscopically, this mass consisted of dense collagen aggregates. B: Tissue from a firm, raised, white mass on a rabbit ear. The dermis is expanded by dense hypocellular bundles of mature connective tissue containing remnants of follicular structures and is covered by mildly hyperplastic epithelium, consistent with a collagen nevus (hamartoma). *Source:* A: Courtesy of The Links Road Animal and Bird Clinic.