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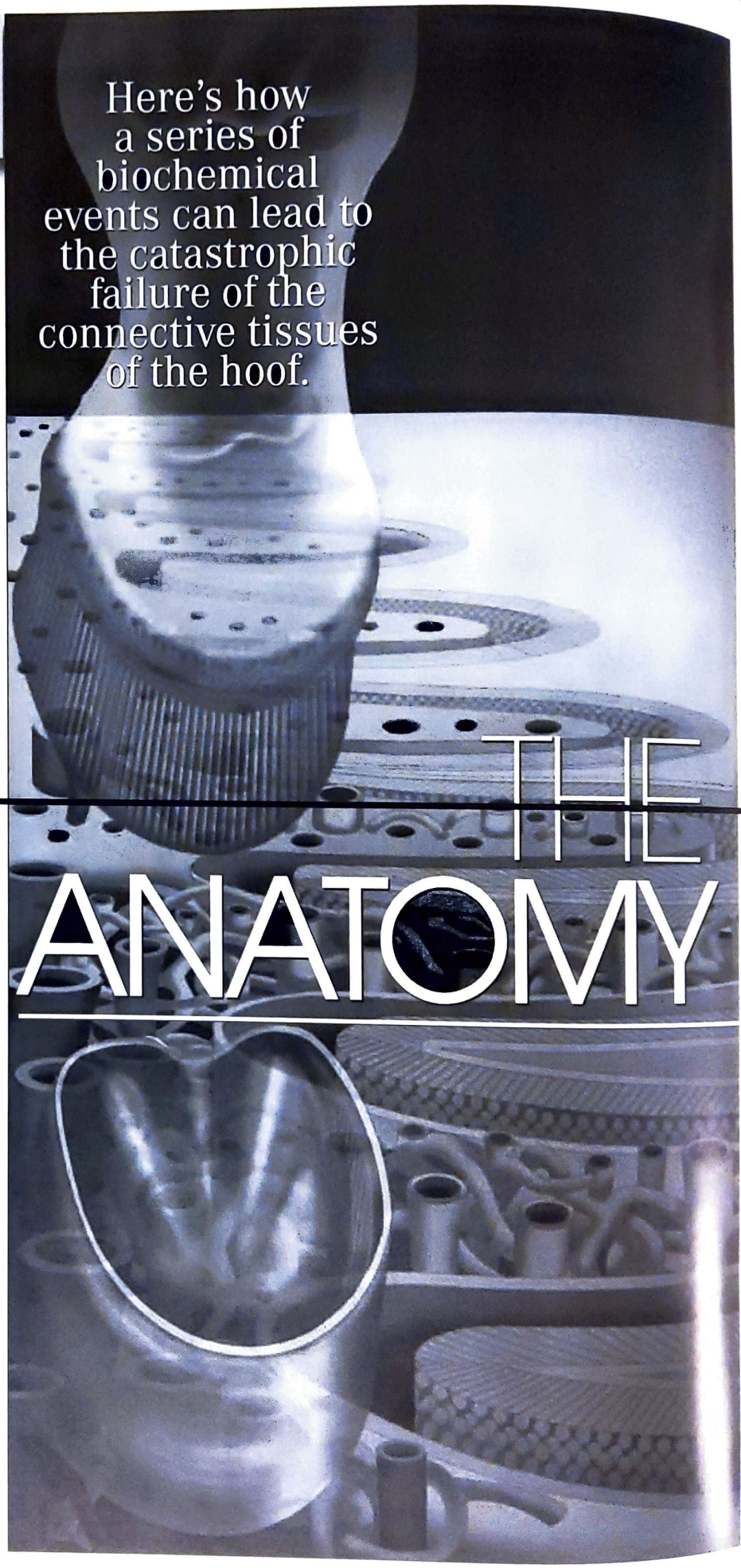
THE ANATOMY

Here's how a series of biochemical events can lead to the catastrophic failure of the connective tissues of the hoof.

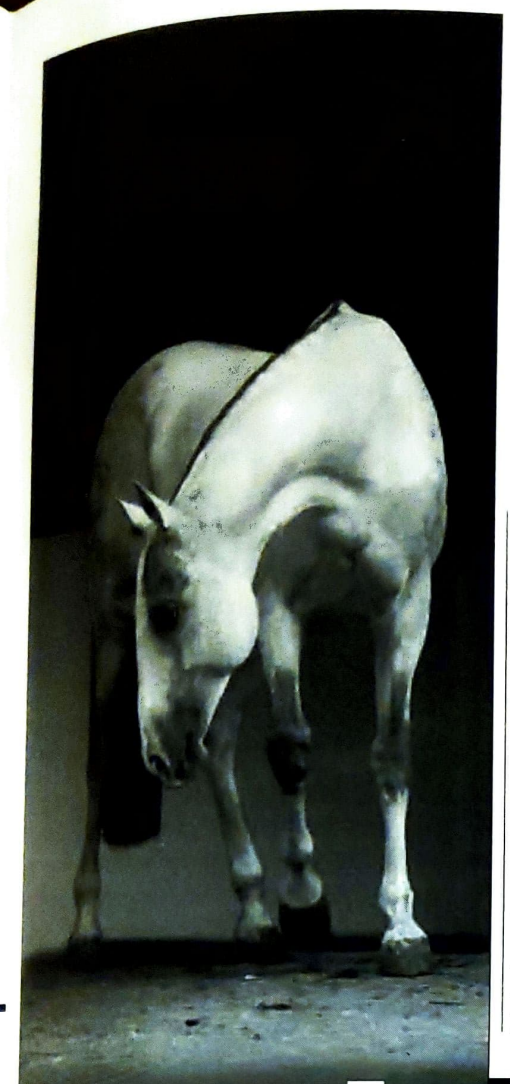


By Laurie Bonner

The equine hoof is remarkably well adapted for its job. A healthy foot can easily withstand the tremendous pounding forces of galloping, pawing, landing jumps and every step a 1,200-pound horse takes.

At first glance it may appear to be hard and solid, yet the hoof is a living, dynamic environment, constantly growing and remodeling to meet the horse's needs. The specific details of many of the hoof's inner workings are still unknown—hidden as it is behind the thick wall, the living tissues inside the hoof can be difficult to study.

But researchers are making progress in understanding what goes on inside a horse's foot, and what can go wrong. Here's a brief overview of the anatomy of a healthy hoof and a look at the events that may lead to the catastrophic failure of connective tissue known as laminitis.



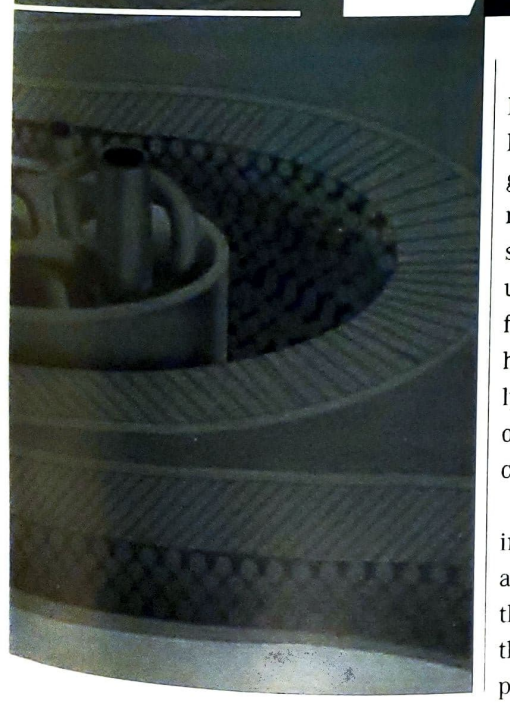
INSIDE THE HOOF

Most of the structures that make up a horse's hoof are related to those in the end of your middle finger: That last joint closest to your fingernail is equivalent to the coffin joint (the distal interphalangeal joint), and that bone under your fingernail is the distal phalanx, also called the third phalanx, coffin bone or pedal bone in the horse. Your fingernail, of course, becomes the horse's hoof wall, a keratinized structure that has expanded to nearly encircle the horse's foot in a conical shape, thickened enough to help bear his weight.

microscopic "secondary laminae," additional tiny pleats that greatly increase their total surface area.

Just as your own skin is made up of an insensitive keratinized layer (epidermis) that lies over and is tightly bound to the sensitive layer (dermis), which is interlaced with capillaries, nerves and other structures, the sensitive primary and secondary laminae in a horse's hoof are covered (interdigitated) with a light-colored tissue called the primary and secondary epidermal laminae (also called the insensitive laminae). These light-colored insensitive laminae are

OF LAMINITIS



The horse's coffin bone, shaped like a miniature hoof, fits inside the hoof wall as neatly as a hand in a glove. Much of the weight of the horse rests upon the digital cushion, the sole and the frog—structures that lie underneath the coffin bone. On its front surface, sides (quarters) and heels, the coffin bone is anchored firmly to—and suspended by—the interior of the hoof wall via the laminae (also called lamellae).

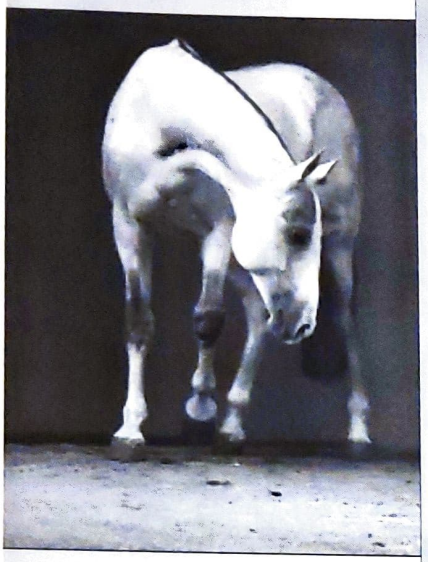
Underneath the hoof wall, these laminae form tiny, narrow "pleats," as many as 600 per hoof, that run parallel from the coronary band to the toe: These are the "primary laminae." Each of these primary laminae is lined with up to 200

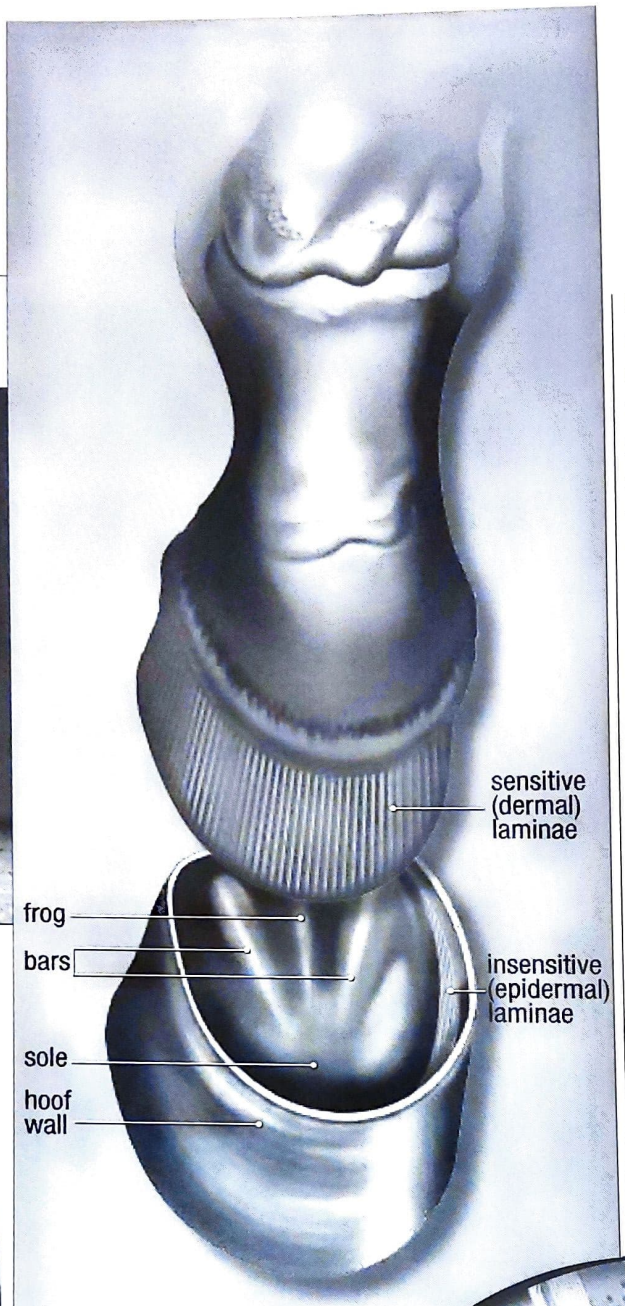
the innermost portion of the hoof wall.

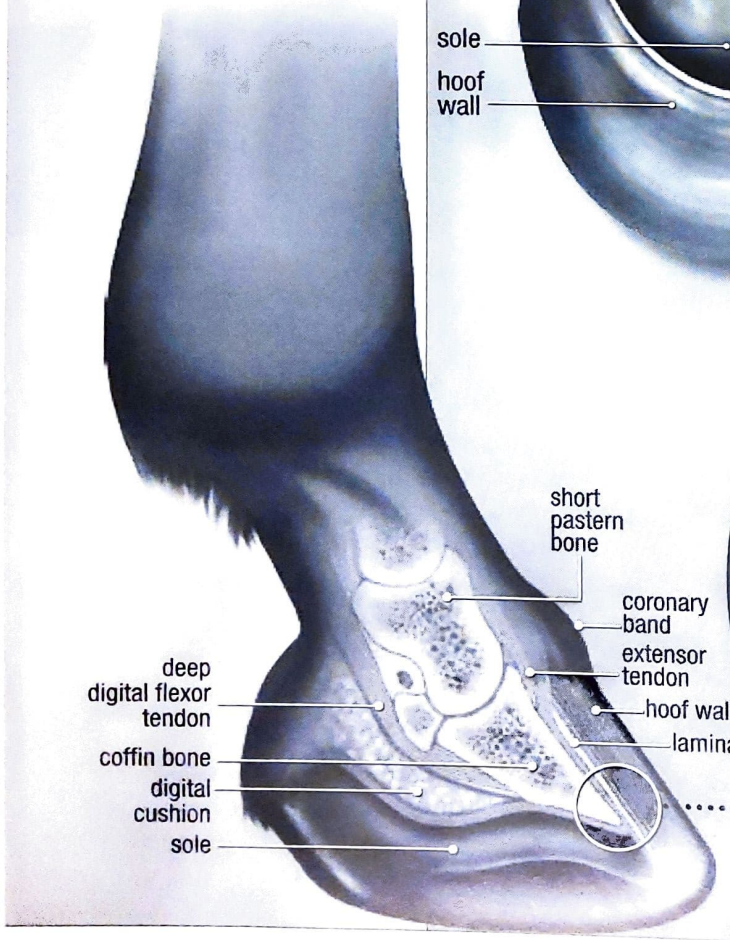
In human skin, the epidermis adheres to the dermis with a structure called the dermoepidermal junction (basement membrane). Similarly, in the hoof, the epidermal laminae consist of an interior layer of cells, the laminar basal epithelial cells, which lie at the interface of the epidermal and dermal laminae and provide the critical attachment to the underlying connective tissue of the dermal laminae.

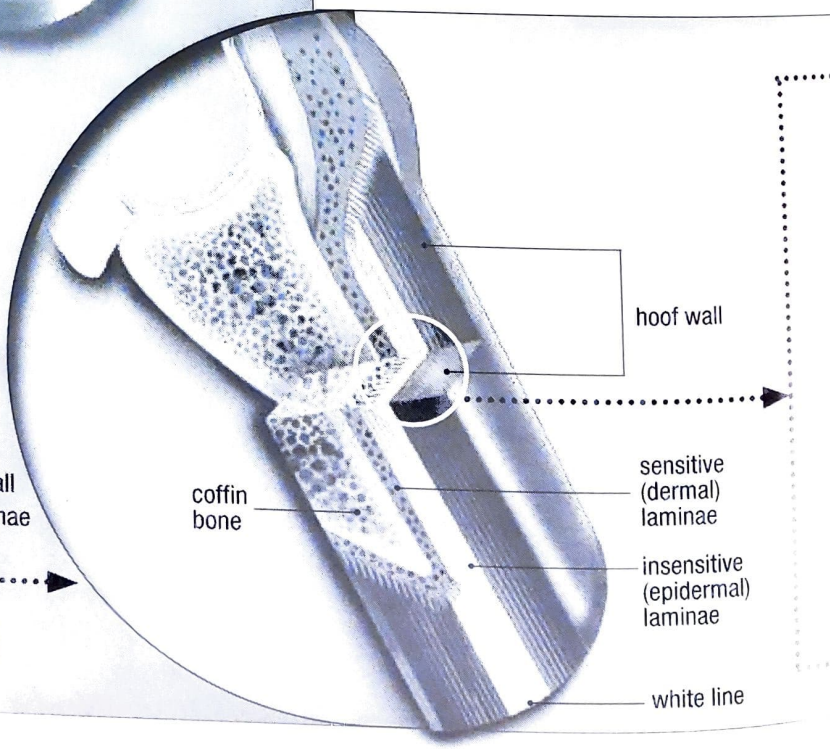
In your skin, the lowest level of the epidermis generates new cells, called keratinocytes, that are dependent upon the circulation from the dermis below for nutrition; as they are continuously replaced with more new

ANATOMY









ILLUSTRATIONS BY CELIA STRAIN

keratinocytes from below, these cells die as they are pushed upward to form the tough outer surface of your skin. In the hoof, too, the innermost layer of the insensitive laminae are actually a few more layers of living epidermal cells, which lie on top of the basal epithelial layer; these cells gradually become more keratinized and finally become continuous with the nonliving, keratinized hoof wall.

The "sensitive," or dermal, laminae are similar to the dermis of our skin. These structures include connective tissue (nonliving proteinaceous fibers of tissue that provide both strength and resilience, or "stretch") interspersed with small blood vessels (called arterioles, capillaries and venules). These blood vessels provide the blood supply not only for the dermal cells of the sensitive laminae but also for the living epidermal cells of the epidermal laminae.

The basal epithelial cells attach to a specialized tissue layer called the basement membrane, which is a tough

sheet of connective tissue interwoven with the connective tissue fibers of the sensitive laminae. The basal epithelial cells are anchored to the basement membrane with structures called hemidesmosomes—specialized protein complexes that start inside the living epithelial cells and pass through the cell membrane to attach to the underlying fibers of the basement membrane with anchoring filaments. These hemidesmosomes act like "rivets" at regular intervals along the surface membrane of the basal epithelial cells, and they are the primary attachment points between the coffin bone and the hoof wall.

It's the interface between the epidermal laminae (attached to the hoof wall) and dermal/sensitive laminae (attached to the coffin bone) that is the focus of laminitis research because this is the connection that undergoes structural failure in laminitis.

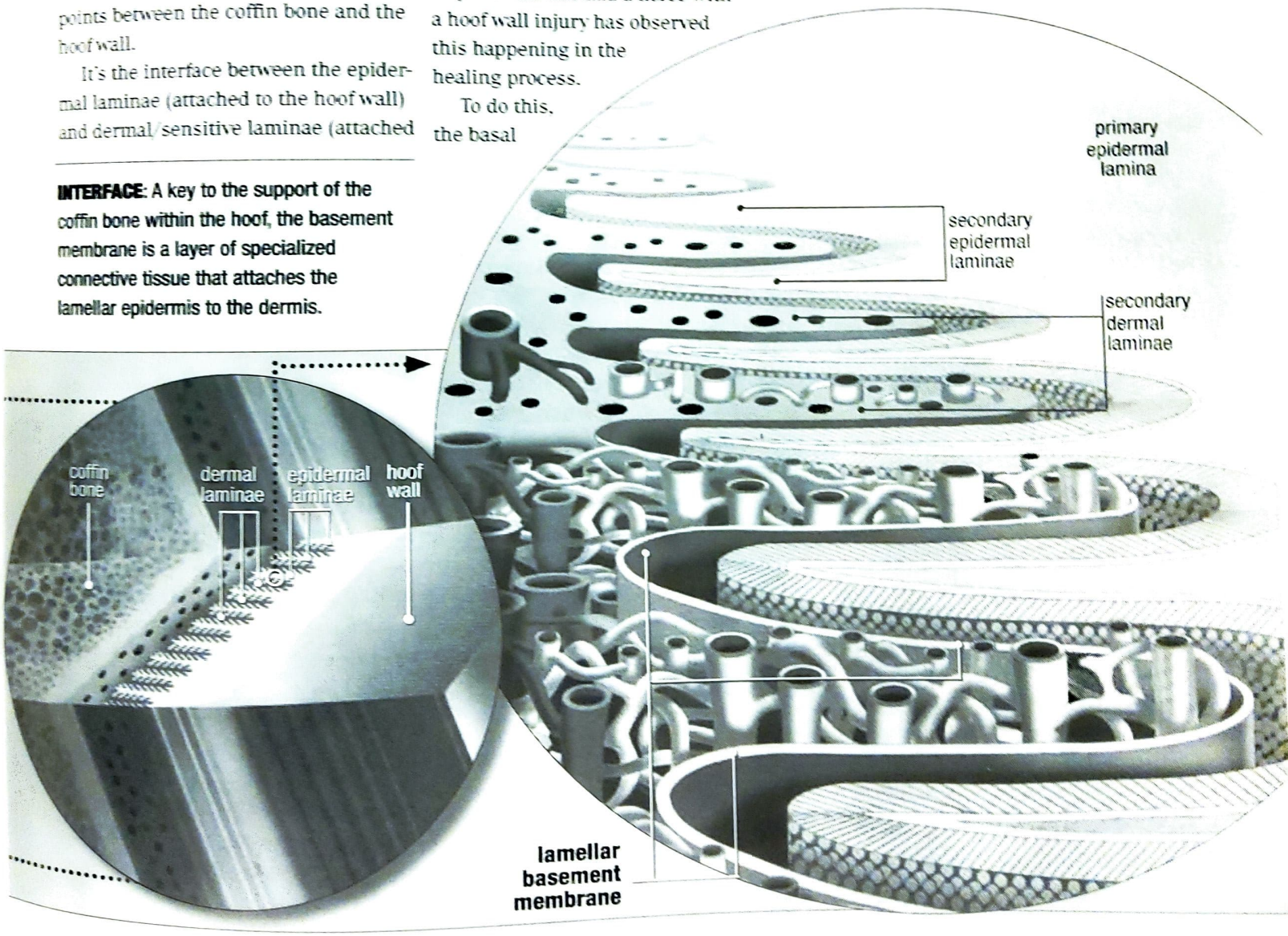
INTERFACE: A key to the support of the coffin bone within the hoof, the basement membrane is a layer of specialized connective tissue that attaches the lamellar epidermis to the dermis.

WHEN THE PROCESS **RUNS AWRY**

Just as your skin heals when you cut or scrape it, the epithelial cells of the hoof evolved to have the ability to heal a wound to the hoof wall: The epithelial cells are able to detach themselves from the underlying basement membrane and migrate across a wound. Anyone who has had a horse with a hoof wall injury has observed this happening in the healing process.

To do this, the basal epithelial cells not only can regulate the formation or dissolution of the hemidesmosomes, they can also release enzymes called matrix metalloproteinases (MMPs), which can break down the connective tissue fibers of the basement membrane. Normally, MMPs are under extremely tight control by three different methods:

- Creation (gene expression) of the proteins is tightly regulated.
- Most of the MMPs need to be cleaved (cut in places) by a second enzyme to be activated.
- A number of proteins, called



tissue inhibitors of metalloproteinases (TIMPs), are normally present in the surrounding tissue and prevent the MMPs from digesting the basement membrane components.

However, if anything were to go wrong with the biochemical signals that keep the MMPs under control, the horse could end up with a sudden overabundance of those enzymes. As a result, the MMPs "unlock" large numbers of hemidesmosome "rivets" all at once, and they can also cause the breakdown of the basement membrane. This weakening of the connection causes large portions of the epithelial cells to lose their grip on the basement membrane within the hoof—this detachment of the epithelial cells is the start of a case of laminitis.

The interface between the epidermal laminae (attached to the hoof wall) and sensitive laminae (attached to the coffin bone) is the focus of research because this is where structural failure occurs in laminitis.

"In humans, if epithelial cells become less adhesive—like with a blister—it's not a big deal, since it would just eventually heal," says James Belknap, DVM, PhD, DACVS, of Ohio State University. "In horses, the laminae are such a critical adhesion, because they bear close to the entire weight of the horse, that as soon as any event affects the attachment of a certain threshold of the basal epithelial cells/laminae, the attachment is going to start failing, and the remaining laminae may start to tear, and then it becomes a wound event, with all of the associated inflammation, etc."

Once that structural failure of the laminae starts, the coffin bone continues to loosen from the hoof wall and can displace toward the ground in three ways:

- If mainly the front of the hoof wall is affected, the leading edge of the coffin bone rotates downward, pulled by the deep digital flexor tendon, which runs down the back of the leg and attaches under the base of that bone; this process is called "rotation."
- If all the laminae around the entire perimeter of the hoof wall are affected to the same degree (which can occur in horses with severe systemic disease), the entire coffin bone can drop symmetrically toward the ground surface; this process is called "sinking" or "distal displacement."
- If only the outside or inside of the quarter and heel attachments fail, the coffin bone can "sink" or "tip" to only one side; this process is called "asymmetrical" or "unilateral" sinking or distal displacement, and it usually happens toward the inside. Although this third type is more rare, it is also a crippling form of the disease and can be missed if your veterinarian takes only the usual lateral (side view) radiograph of the foot. This type of displacement can be observed only on a front-to-back view (dorsopalmar or anterior-posterior).

The displacement of the coffin bone—called founder—can be mild, with a shift of only a few millimeters, or severe. In extreme cases of rotation (or rotation combined with sinking), the leading edge of the bone may penetrate through the sole of the hoof. This severe a displacement of the coffin bone requires drastic procedures to save the horse. New solar tissue will grow over the bone if the treatment is successful, but it can be difficult to restore the bone to its original position.

A classic case of acute laminitis occurs in multiple stages:

- The developmental phase is the point at which laminar injury (and possibly slight detachment of the dermal laminae from the epidermal laminae/hoof wall) begins. Usually, the horse is not yet showing any outward signs of hoof pain or lameness, although he may be ill from other causes. In cases monitored when laminitis is induced in the laboratory, the developmental phase can last 24 to 40 hours.
- The acute phase begins as soon as the horse shows the first signs of foot pain and lameness and continues until the coffin bone starts rotating and becomes displaced. Other signs at this stage include an exaggerated, "bounding" pulse in the arteries above the fetlock and noticeable heat around the coronary band and hoof. Not all horses with laminitis—that is, those who've experienced detachment of the epithelial cells—will also develop displacement of the bone, especially if they are treated promptly with measures including padding the underside of the feet.
- A horse who survives the acute disease may recover completely, or, if the process cannot be halted, will develop chronic laminitis, a term that is used to describe the ongoing pain and soundness issues caused by the crippling displacement of the coffin bone within the hoof wall. The new epithelial attachments that form as the hoof wall grows out will be weaker than before, and the horse will be prone to recurrent laminitis. Sometimes, recurrent cases may actually be flare-ups of ongoing low levels of disease in a horse's laminae; this is common in

6 WAYS TO PREVENT LAMINITIS

Although the threat of laminitis looms larger with certain horses, it's wise to take steps to protect every horse in your care.

1. Limit access to lush pasture, particularly for at-risk horses. The majority of laminitis cases are caused by too much lush pasture, particularly in the spring and fall when grass can be high in fructan, the triggering sugar. How much grass is "too much" depends on the individual horse, so there's no hard and fast prescription for safe grazing in the spring. Discuss your horse's laminitis risk profile with your veterinarian and err on the side of caution, using grazing muzzles or moving him to a dry lot if necessary when pastures are lush.

2. Reduce the carbs and sugars in your horse's diet. If your horse has had laminitis, is insulin resistant or is otherwise at risk, minimize the sugars and starches in his diet, swapping molasses-based sweet feeds for a low-sugar formulation, for instance. Most feed companies produce at least one product specifically for laminitis prevention. Also remember that treats—even seemingly "healthy" ones—can be high in sugars: Offer your horse carrots instead of peppermints or apples.

3. Keep hooves in good shape. Overgrown and unbalanced hooves can develop mechanical laminitis. Neglected hooves are also less able to withstand even minor metabolic insults, making them more likely to progress to founder than healthier hooves. Have your horse attended to regularly (every six to eight weeks) by a qualified farrier.

4. Don't let Cushing's go unchecked. A malfunction of the pituitary gland that causes excess production of the hormone cortisol[0], Cushing's[0] disease is common in horses over the age of 20. Signs include a coat that is slow to shed, muscle wasting, increased thirst and lethargy, but the real danger comes from a heightened susceptibility to laminitis. Have your veterinarian test your older horse for Cushing's and, if necessary, begin daily treatment with the drug pergolide to mitigate the harmful effects.

5. Watch his weight. The relationship between obesity, metabolic dysfunction and laminitis is complex, but one thing is clear: Overweight horses are far more likely to develop the condition. Consult with your veterinarian to get an unbiased opinion of your horse's body condition and, if necessary, devise a diet and exercise plan that safely slims him down.

6. Protect his "good" limbs after an injury. If a serious orthopedic injury causes a horse to bear more weight than usual on a particular limb, the risk of laminitis in that hoof increases. As part of treatment for any orthopedic injury, most veterinarians support the opposite limb in some manner, such as with wraps or Styrofoam supports underneath the sole. If your horse sustains a severe orthopedic injury, follow through with any preventive measures your veterinarian puts in place. You may be tempted to focus solely on the injury, but attention to the unaffected limbs is just as critical.

horses and ponies with endocrinopathic laminitis.

The term "chronic laminitis" can also be used to describe cases that come on gradually, usually in horses who are grazing lush pasture or have a metabolic disorder such as a pituitary tumor. The horse may have mild lameness or just be generally footsore for months or years; in these cases, x-rays may show evidence of slight bone rotation that had gone undetected.

WHAT GOES **WRONG?**

So what exactly causes the epithelial cells to detach from the basement membrane? What biochemical pathways are going awry and upsetting the balance that keeps the attachments strong? Why does this happen?

These are among the more important questions researchers are currently trying to answer. "There is fairly good evidence that laminitis involves the dissolution of the hemidesmosomes, but we don't yet know what pathway leads to that event," says Belknap. "In fact, it's becoming clear that there can be more than one pathway."

Once further research identifies the biochemical cascades that can affect the hemidesmosomes and the connective tissues within the horse's foot, the goal would be to find ways not only to prevent laminitis, but to treat it more effectively when it occurs. With recent advances in biomedical research techniques, those goals may well be coming within reach in years to come.

EQUUS thanks James Belknap, DVM, PhD, DACVS, of Ohio State University for his assistance in the preparation of this article. In addition to researching laminitis, Belknap is a practicing equine surgeon, working with two Journeyman farriers on podiatry cases.