AMERICAN HEALTH CONSULTANTS®

Rapid Reference Card Enclosed

Log on to www.EMRonline.com, your source for emergency medicine information

The Practical Journal for Emergency Physicians

Emergency Medicine Reports

Volume 23, Number 23

November 4, 2002

The Acute Hand: Assessment and Management in the ED Setting

Part I: Anatomy, Assessment, and Initial Management

Author: **Gary D. Hals, MD, PhD**, Attending Physician, Department of Emergency Medicine, Palmetto Richland Memorial Hospital, Columbia, SC.

Peer Reviewers: **Alasdair K.T. Conn, MD**, Chief of Emergency Services, Massachusetts General Hospital, Boston; **Andrew D. Perron, MD, FACEP**, Assistant Professor of Emergency Medicine, Associate Residency Director, Department of Emergency Medicine, University of Virginia, Charlottesville.

The human hand is an amazing tool, resulting from millions of years of evolutionary fine-tuning. It is capable of precise movements of less than a millimeter and, at the same time, possesses great strength and flexibility. One only needs to look at our woefully inadequate attempts to replicate or replace a hand to understand how complex hands really are. Unfortunately, as our hands are used for so many purposes, they are the parts of the body most often placed in the environment and, therefore, commonly are injured. In fact the bones of the hand are the most commonly fractured bones in the body,[1] with the fingers being the most common site of hand bone fractures.[2] Other hand problems frequently present to the emergency department (ED), as well: infections, dislocations, tendon lacerations, burns, bite wounds, etc. The ED physician must be aware of which problems can be managed in the ED and which require urgent or emergent consultation by an experienced hand surgeon.

Hand injuries account for between 5% and 10% of overall ED visits,[3] or approximately 11 million injuries in the United States each year.[4] Many people from surgeons to musicians to carpenters rely heavily on proper hand function to make a living. Disability from permanent loss of normal hand function can be devastating, and, unfortunately, is not a rare event. Hand injuries are among the leading cause of occupational injury in the United States,[5] and account for 30% of all injuries at work.[4] Work-related hand problems make up one-third of all chronic injuries, 25% of lost time at work, 20% of permanent disabilities[6] and 75% of partial disabilities.[4] Prevention of permanent hand damage and disability often starts with correct diagnosis and treatment of acute hand injuries in the ED. For example, tendon lacerations easily are missed, resulting in delayed care and limited range of motion. Angulated fractures must be recognized early and given proper reduction to restore hand function. In some cases, however, only when the patient's hand is examined through its entire range of motion will the deformity be apparent. Deep-space hand infections often can begin in the palm but present with maximal findings on the dorsal surface. Clenched fist injuries, or "fight bites," are probably one of the best examples of a common injury that will produce serious complications if not recognized and ade-

quately treated on the first presentation. For many acute hand problems, proper diagnosis by the emergency physician is crucial so that the patient does not leave the ED after inadequate treatment that could lead to preventable complications. Many texts on hand injuries assert the importance of the initial care of hand injuries. "The fate of the hand largely depends on the judgement of the doctor who first sees the patient. The initial evaluation and care of the injured hand is critical, for at that time the surgeon has his best opportunity to assess accurately the extent of the damage and to restore the altered anatomy," according to Green and Rowland.[7] As the emergency physician typically is the first physician to treat hand problems, correct evaluation, initial treatment, and proper referral rests on our shoulders. With this in mind, this paper will cover the spectrum of acute hand problems. Basic relevant anatomy will be reviewed followed by a discussion of ED diagnosis and management of hand infections and the variety of hand trauma that can present to the ED. Unique hand injuries, such as high-pressure injection injuries and fight bites, also will be discussed. Basic laceration repair will not be discussed specifically, but the ED physician should rule out injury to deep structures as a part of any hand laceration repair. Part I of this three-part series will cover anatomy, assessment, and initial management. Parts II and III will cover fractures, dislocations, tendon injuries, amputation, and infections.

—The Editor

Anatomy

Terminology. The hand's unique function and abilities arise directly from its anatomy. When dealing with hand problems, knowledge of anatomy is crucial; the physician must know where nerves, tendons, and arteries are located to be suspicious of their injury. The physician must assume all structures deep to a wound are involved until proven otherwise. It also is important to know and use the proper terms ("handspeak") when discussing a case with a consultant. Although terminology of the hand is relatively simple, some authors refer to the phalanges by number with the thumb being 1 and the little finger being 5; it is equally acceptable, and sometimes less confusing, to refer to them by name: thumb, index, middle, ring, and little fingers. At the distal interphalangeal (DIP), proximal interphalangeal (PIP), and the metacarpophalangeal (MP) joints, the bones are connected by two collateral ligaments (radial collateral and ulnar collateral). On the palm (volar) surface, the joints are connected by the volar plate, a strong fibrocartilaginous band. (*See Figure 1.*) This arrangement allows for maximal flexion and stability in that range of motion. When a hand joint is dislocated, one or more of these ligaments will be disrupted, either partially or completely. It is important to test the joint stability after reduction. The hand often is divided into zones when discussing tendon injuries, but different systems are used for flexor and extensor tendons. The hand and wrist are divided into seven zones for extensor tendons but only five for flexor tendons. (*See Figures 2a and 2b.*) Verdan's classification system is most widely accepted for describing extensor tendons.[9]

Flexor Tendons. The flexor tendons are more complicated than the extensor tendons, because there are two flexors and only one set of extensors for each digit. The thumb is the exception, with only one flexor, as it has only one interphalangeal (IP) joint to move. The thumb flexor is flexor pollicis longus (FPL), which inserts on the distal phalanx just above the IP joint. Flexor digitorum superficialis (FDS) and flexor digitorum profundus (FDP) originate in the forearm muscles and travel to each finger. FDS inserts on the middle phalanx, while FDP inserts on the distal phalanx just above the joint. Thus, FDS acts to flex only the PIP joint, while FDP is the primary flexor in the hand and acts to flex both the PIP and DIP joints. It is important to realize that the FDS can be severed completely and there still will be active flexion at both joints from the intact FDP. As would be suspected from their names, FDS runs superficial to FDP in the hand. This changes at the level of the proximal phalanx, where FDS splits in half and

Emergency Medicine Reports™ (ISSN 0746-2506) is published biweekly by American Health Consultants, 3525 Piedmont Road, N.E., Six Piedmont Center, Suite 400, Atlanta, GA 30305. Telephone: (800) 688-2421 or (404) 262-7436.

Vice President/Group Publisher: Brenda Mooney
Editorial Group Head: Valerie Loner
Specialty Editor: Shelly Morrow
Marketing Manager: Schandale Kornegay
GST Registration No.: R128870672

Periodicals postage paid at Atlanta, GA. **POSTMASTER:** Send address changes to ***Emergency Medicine Reports***, P.O. Box 740059, Atlanta, GA 30374.

Back issues: $29. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

Multiple copy prices: One to nine additional copies, $323 each; 10 to 20 additional copies, $287 each.

Accreditation

Emergency Medicine Reports'™ continuing education materials are sponsored and supervised by American Health Consultants. American Health Consultants designates this continuing education activity for up to 52 hours in Category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

This CME activity was planned and produced in accordance with the ACCME Essentials.

Emergency Medicine Reports™ also is approved by the American College of Emergency Physicians for 60 hours of ACEP Category 1 credit and has been approved for 52 Category 2B credit hours by the American Osteopathic Association. Emergency Medicine Reports has been reviewed by the American Academy of Family Physicians as having educational content acceptable for Prescribed credit hours. This volume has been approved for up to 60 Prescribed credit hours. Term of approval covers issues published within one year from the beginning distribution date of 1/02. Credit may be claimed for one year from the date of this issue.

American Health Consultants (AHC) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

This is an educational publication designed to present scientific information and opinion to health professionals, to stimulate thought, and further investigation. It does not provide advice regarding medical diagnosis or treatment for any individual case. It is not intended for use by the layman. Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement. Clinical, legal, tax, and other comments are offered for general guidance only; professional counsel should be sought for specific situations.

Subscriber Information

Customer Service: 1-800-688-2421

Customer Service E-Mail: customerservice@ahcpub.com
Editorial E-Mail: shelly.morrow@ahcpub.com

World Wide Web page: http://www.ahcpub.com

Subscription Prices

1 year *with* 60 ACEP/60 AMA/60 AAFP Category 1/Prescribed credits (52 AOA Category 2B credits): $524
1 year *without* credit: $379
Resident's rate $189

All prices U.S. only.
U.S. possessions and Canada, add $30 plus applicable GST. Other international orders, add $30.

For Customer Service and CME questions,

Please call our customer service department at **(800) 688-2421.** For editorial questions or comments, please contact **Shelly Morrow,** Specialty Editor, at shelly.morrow@ahcpub.com or (404) 262-5514.

THOMSON
AMERICAN HEALTH CONSULTANTS

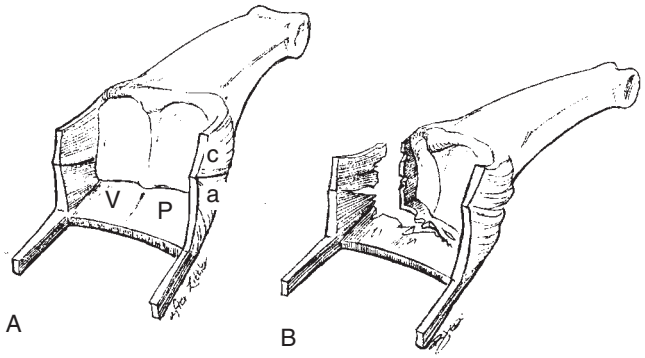
Statement of Financial Disclosure

In order to reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, we disclose that Drs. Hals (author), Conn, and Perron (peer reviewers) report no relationships with companies related to the field of study covered by this CME program. Dr. Bosker (editor) is on the speaker's bureau for Pfizer, Aventis, Bayer, and Hoffman-La Roche. Dr. Bosker also acknowledges that he receives or has received royalties, honoraria, commissions, and other compensation relating to the sale of textbooks, consultation services, reprints of articles, and other written materials to the following pharmaceutical companies: Pfizer, Genentech, Aventis, Ortho-McNeil, Pharmacia, Hoffman-La Roche, and Bayer.

runs in ulnar and radial halves until they insert on the middle phalanx. (*See Figure 3.*) FDP emerges through the split in FDS and from the middle phalanx runs as the single tendon to its insertion on the distal phalanx. This relationship is important to remember when evaluating finger lacerations for tendon involvement. The physician must know how many tendons there are beneath the laceration to adequately identify injuries to them. In other words, when exploring a laceration at the proximal phalanx, if one sees only a single intact tendon, this means FDS has been transected completely. If the physician is unaware that two intact tendons should be present, he could misdiagnose the injury, with potentially disastrous results. A series of fibrous bands called "pulleys" are present in all the fingers and act to prevent bowing of the flexor tendons when the finger is flexed. (*See Figure 4.*) The pulleys are made by thickenings of the synovial sheath surrounding each flexor tendon. A2 and A4 are considered essential pulleys, because without them, significant bowstringing will occur. These pulleys also can be torn with or without tendon injury, and A2 or A4 injuries are important to identify. The synovial sheaths covering the flexor tendons contain synovial fluid that acts to lubricate the tendon's movements and supply nutrients to the avascular tendons. (*See Figure 5.*) The presence of the tendon sheaths also provides a pathway for spread of infection (flexor tenosynovitis).

Extensor Tendons. In comparison to the rounded flexor tendons, the extensor tendons are broad and flat. The extensor tendon system is less complicated in that there is a single set of extensor tendons and there is no pulley system or tendon sheath above the wrist. The fibrous extensor retinaculum at the wrist prevents bowstringing of extensor tendons when the wrist is extended. There are, however, nine extensor tendons in six compartments on the dorsum of the hand. The first compartment contains extensor of the thumb: abductor pollicis longus (APL) and extensor pollicis brevis (EPB). APL inserts on the base of the first metacarpal and acts to radially abduct the thumb. EPB inserts on the base of the proximal thumb phalanx and extends the thumb at the MP joint. The second compartment also contains two wrist extensors: extensor carpi radialis longus and brevis. The third compartment contains extensor pollicis longus (EPL). EPL inserts on the distal thumb phalanx and acts to extend both the IP joint and MCP joint of the thumb. It is important to realize that because abductor pollicis brevis and adductor pollicis add some extension to the thumb, as a patient with complete laceration of EPL still may have some thumb extension on exam. The fourth compartment contains the tendons that extend the fingers: extensor indicis proprius (EIP) and extensor digitorum communis (EDC). EDC divides into four tendons after it passes through the extensor retinaculum and sends a separate tendon to the index, middle, ring, and little fingers. The complex attachment of the EDC to the dorsal phalanx is shown in Figure 6. Important points from this figure include the following: Disruption of the central slip mechanism will produce an acute boutonniere deformity, while rupture of the oblique retinacular ligament causes a swan-neck deformity. Given the complex nature of the extensor mechanism in the finger, meticulous repair is essential to preserve proper finger function.

Figure 1. Close-up of Collateral Ligaments and Volar Plate



This diagram shows a close-up of collateral ligaments (a and c) and volar plate (VP) surrounding the finger joints. This box-like shape allows for maximum movement and stability of the joint. This figure shows how the ligaments and volar plate can be torn in dislocation.

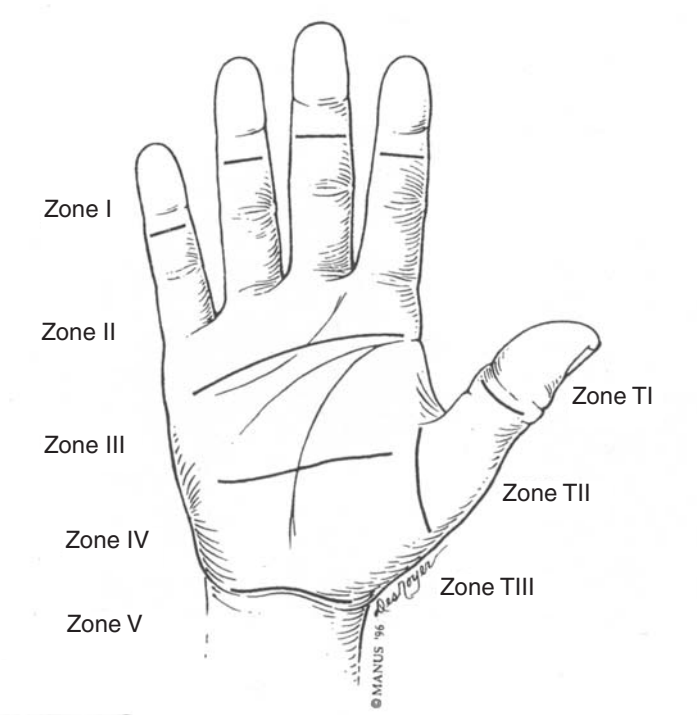
Reprinted with permission: Rosen P, Barkin R, Hockberger R, et al., eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. St. Louis: Mosby;1999:638.

Fibrous connections called juncturae tendinae attach the four branches of EDC on the dorsum of the hand. When evaluating finger extension, it is important to understand that the juncturae tendinae aid in finger extension and in some patients will provide normal extension of a finger even in the face of complete laceration of the EDC distal to them.[10] The juncturae tendinae also prevent significant proximal retraction of the tendon when lacerated. EIP is a second extensor tendon for the index finger. The little finger also has a second extensor, extensor digiti quinti, which is housed in the fifth compartment. The dual extensor system for the index and little finger provide them with considerable independent extension, whereas the middle and ring finger have limited independent extension. The sixth compartment holds the extensor carpi ulnaris, which ulnarly deviates and extends the wrist.

Intrinsic Hand Muscles. The intrinsic muscles of the hand include the lumbricals, interosseous, thenar, and hypothenar muscles. The lumbricals originate from the FDP and insert on the proximal phalanx just above the MP joint. They act in flexion of the MP joints and extension of the PIP joints, and are the primary muscles that provide these movements. Their connection to the proximal phalanx forms a complex combination with the EDC tendon. (*See Figure 6.*) The interosseous muscles are found between the metacarpals. The dorsal interosseous muscles abduct the digits, while the volar interosseous muscles adduct them. The thenar muscles (abductor pollicis brevis, flexor pollicis brevis, and oppenens pollicis) perform thumb abduction and serve in opposition to the other digits. The hypothenar muscles (abductor digiti minimi, flexor digiti minimi, and oppnens digiti minimi) function in abduction and opposition of the little finger.

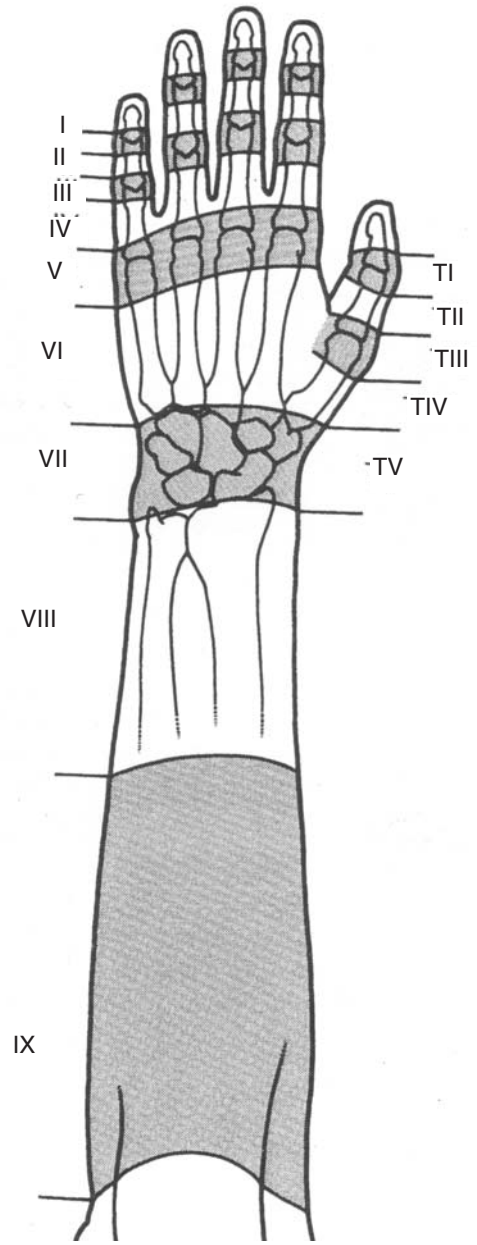
Arteries. The radial and ulnar arteries provide blood supply to the hand. The radial artery runs radial and deep to the flexor

Figure 2A. Zones of Flexor Tendons



Reprinted with permission: Green DP. *Green's Operative Hand Surgery*, 4th ed. Philadelphia: Elsevier Science; 1999:1857.

Figure 2B. Zones of Extensor Tendons



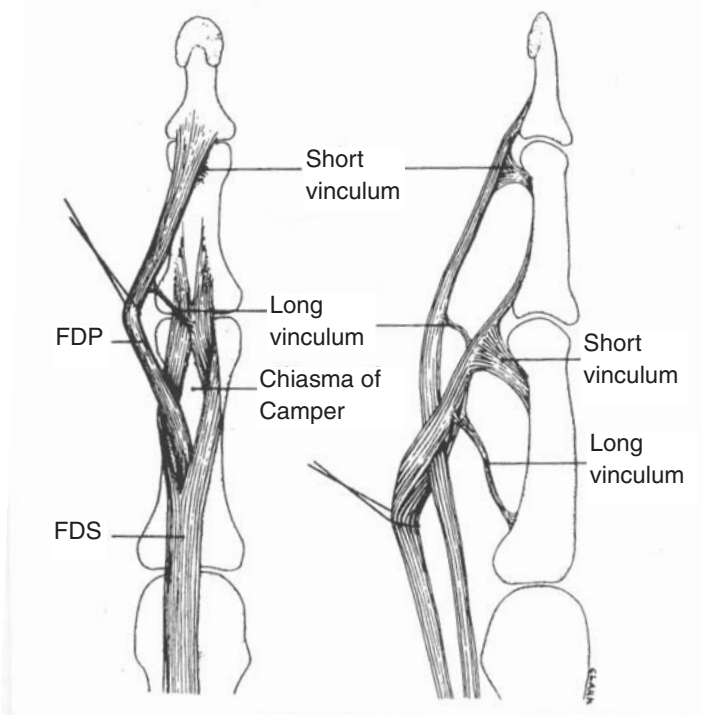
Reprinted with permission: Green DP. *Green's Operative Hand Surgery*, 4th ed. Philadelphia: Elsevier Science;1999:1956.

carpi radialis tendon. Its pulse easily is assessed in the wrist. The ulnar artery lies deep to the flexor carpi ulnaris and adjacent to the ulnar nerve. The proximity of the ulnar nerve and artery make isolated injuries of either structure rare. Evidence of injury to one structure should be interpreted to mean that both are involved until proven otherwise. The ulnar artery supplies the superficial palmar arch, while the radial artery is the principal supply of the deep palmar arch. To complicate matters, both arches usually are connected to both arteries and to each other, with only one artery providing the dominant supply. Arches also can be incomplete in that they lack the normal connections. A recent study of arterial patterns found that complete arches were present in only 84% of individuals studied.[11] Although it varies in each individual, the ulnar artery (through the superficial arch) usually is the dominant source of hand perfusion. The Allen test can be performed to assess if the hand has independent perfusion by the radial or ulnar artery. (*See section on Examining the Acute Hand and Figure 7.*)

The digits each have a dual blood supply with an ulnar and a radial digital artery arising from converging branches of the superficial and deep palmar arches. Like the ulnar artery and nerve in the wrist, the digital arteries and nerves run parallel to each other in the fingers, and injury to either structure should indicate both are involved until proven otherwise. Even when one digital artery is lost, adequate blood flow usually remains, so repair of a single digital artery is not indicated in the presence of good clinical perfusion.

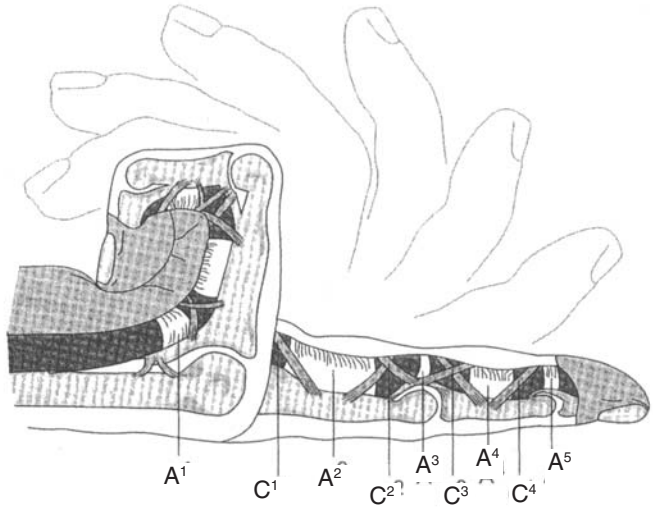
Nerves. Three nerves supply the hand: radial, median, and ulnar. The radial nerve in the hand is purely sensory, while the median and ulnar are mixed motor and sensory nerves. The radial nerve supplies the extrinsic wrist and hand extensors, but supplies no intrinsic hand muscles. These muscles allow wrist and MP joint extension as well as thumb extension and abduction. The radial nerve does supply sensation to the proximal dorsal aspect of the thumb, index, on middle fingers and half the ring finger. At the level of the forearm, the median nerve innervates FDS, the radial part of FDP, and FPL. After passing through the carpal tunnel, the recurrent branch innervates the abductor pollicis brevis, opponens pollicis, and, in some people, flexor pollicis brevis. Digital branches of the median nerve innervate lumbricals for the index and middle fingers. The median nerve pro-

Figure 3. Insertions of Flexor Digitorum Superficialis and Flexor Digitorum Profundus Tendons in the Finger



FDS = Flexor Digitorum Superficialis
FDP = Flexor Digitorum Profundus
Note that FDP becomes superficial to FDS in the proximal phalanx.
Reprinted with permission: Rosen P, Barkin R, Hockberger R, et. al, eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. St. Louis: Mosby; 1999:634.

Figure 4. Flexor Tendon Pulleys



This drawing of the flexor tendon pulleys shows how they function to prevent bowstringing of the flexor tendon with finger flexion. The A2 and A4 pulleys are considered essential ones.
Reprinted with permission: Rosen P, Barkin R, Hockberger R, et. al, eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. St. Louis: Mosby; 1999:634.

vides sensation for the radial two-thirds of the palm, and the palmar surface of the thumb, index, on middle fingers and half of the ring finger. It also supplies sensation for the distal section on the dorsal index on middle fingers and half of the ring finger. Substantial variation in the sensory distribution of the median and ulnar nerves can exist. (*See section on Examining the Acute Hand.*)

The ulnar nerve is critical for proper hand function. It innervates the hypothenar muscles, seven interosseous muscles, lumbricals for the ring and little fingers, adductor pollicis, and both flexors to the ring and little fingers. Loss of ulnar nerve function will destroy the pinching action of the index finger and thumb. Sensation for the entire ulnar side of the hand, entire little finger, and half the ring finger is provided by the ulnar nerve.

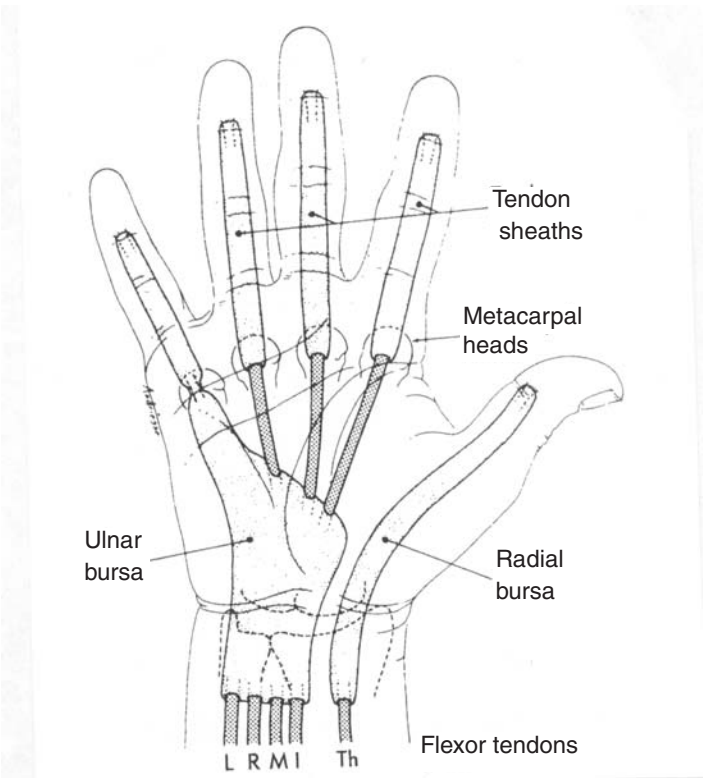
Examining the Acute Hand

Prior to a full hand exam, a brief directed history should be obtained. This information often will be crucial for the hand consultant and should not be overlooked. The following information will be needed: detailed history of the complaint (time since onset, functional impairment, mechanism of injury, etc), hand dominance, occupation (and important hobbies), medical illnesses, last food and drink, allergies, previous injury or treatment of the affected hand, any current medications (especially antibiotics "borrowed" from another), tobacco use (important for revascularization), and tetanus status.

The following sections assume that one is dealing with an isolated hand problem, and that, in the case of multiple injuries, proper attention to advanced trauma life support principles already have been given. One must be aware that traumatic hand injuries can be accompanied by initially occult but more serious injuries. Gunshot wounds (GSWs), industrial accidents, knife injuries, motor vehicle accidents (MVAs), and assault are just some of the instances in which distressing and conspicuous damage to the hand potentially can divert the physician's attention away from higher-priority problems. The physician must be sure to evaluate the patient for life-threatening injuries before focusing on the acute hand injury. Do not forget to fully examine the rest of the patient and adhere to airway, breathing, and circulation (ABCs) in every case to avoid unnecessary risk for the patient.

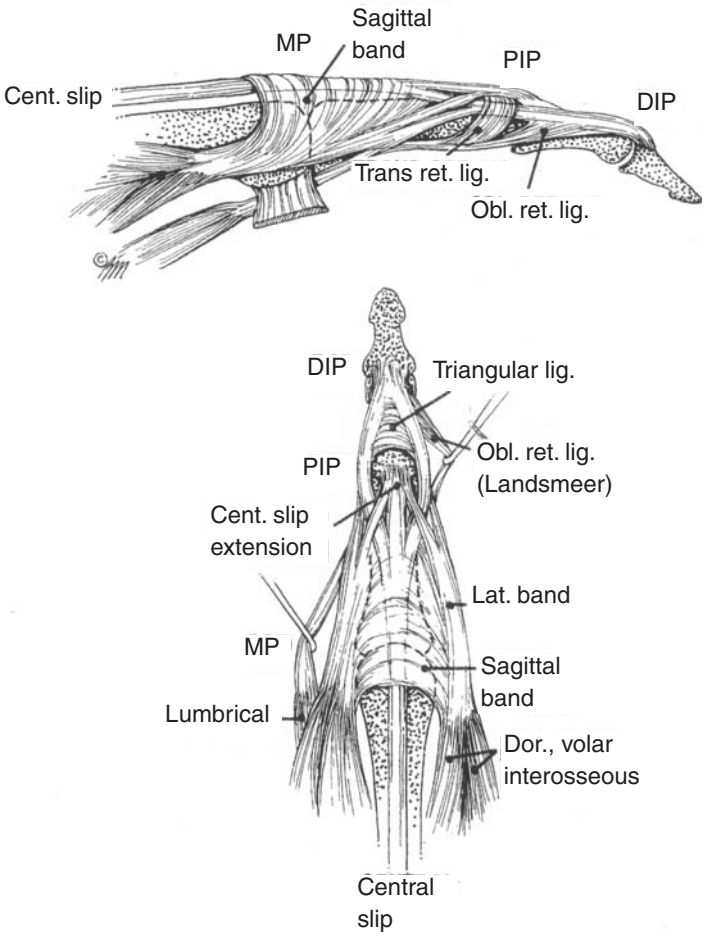
Initial Evaluation. In many situations, such as advanced infection or significant trauma, the patient can be in considerable distress from pain. The patient should be reassured that after a brief (and necessary) exam his or her discomfort will be treated humanely and without any avoidable delay. Anesthesia (local, digital block) never should be provided without first performing an adequate exam (especially of sensory function). The hand consultant's treatment often hinges on the results of the initial exam, and this information can be lost or greatly delayed by well-intentioned but inappropriately timed anesthesia.

Figure 5. Flexor Tendon Sheaths and Bursae



Reprinted with permission: Rosen P, Barkin R, Hockberger R, et. al, eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. St. Louis: Mosby;1999:635.

Figure 6. Insertions of Extensor Tendons in the Finger



This figure shows how complex the relationship is between the extensor tendon and its attachments in the finger.
Reprinted with permission: Rosen P, Barkin R, Hockberger R, et. al, eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. St. Louis: Mosby;1999:633.

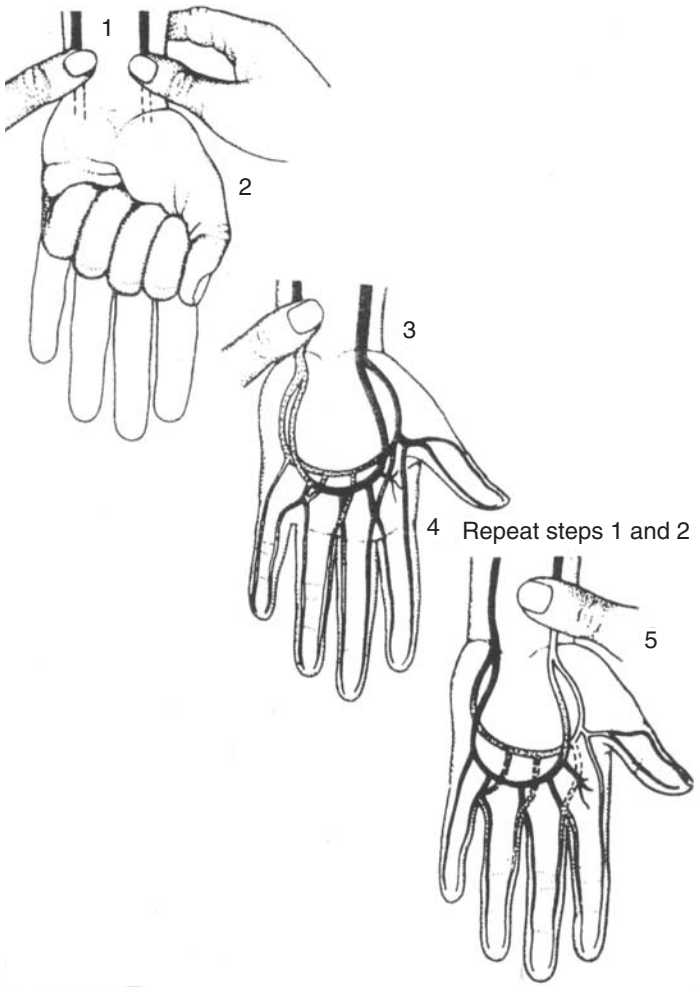
The initial hand exam begins with observation of the two hands, after removal of any rings or other jewelry to avoid potential circulatory compromise. Much can be deduced from just this simple maneuver. Look at the resting position of the affected hand in comparison to the unaffected side (assuming a single hand is involved—for bilateral problems the hands can be compared to the resting position of your own hand). Comparison with the patient's normal hand can make swelling, bruising, pallor, deformity, etc., easier to appreciate. Tendon damage also will be apparent from changes in the normal lie of the hand. Normally, the fingers will be in a cascade of increasing flexion with the little finger having the most flexion. The MP joints are at approximately 45° of resting flexion, around 30-40° at the PIP joints, and 10-20° at the DIP joints. The IP joint of the thumb rests at 10-20°, similar to the DIP joints. Loss of an extensor tendon will produce an exaggeration of flexion as loss of a flexor tendon will give a pronounced extension at rest. This change in position is very reliable with complete tendon lacerations, but incomplete lacerations may not show changes at rest.

Vascular Status. It is very important to remember that blind clamping of a bleeding vessel never should be done to control bleeding in the hand. Nerves and tendons can be crushed unintentionally and permanently damaged in the process. Bleeding of the hand can be controlled with direct pressure or through inflation of a blood pressure (BP) cuff for temporary control. Inflate the cuff to 30 mmHg above systolic pressure, but release periodically after every 30 minutes to alleviate ischemic pain. Even with complete transection of an artery, bleeding usually will stop spontaneously from constriction and retraction of the vessel. Often this occurs before presentation to the ED, and one should not be misled by a benign presentation. Remain suspicious of arterial injury if the history (blood "shooting into the air," etc.) and location of injury are consistent with such an injury.

A significant arterial injury often will present with marked pallor or cyanosis of the affected digit(s). Capillary refill can best be assessed under the nail, and will be slowed in digits with decreased arterial supply. The radial pulse in the wrist should be felt, and the ulnar pulse assessed with a Doppler signal if unable to be palpated. Normal pulses are 2+, with 1+ describing a distinct but weaker pulse than normal. Likewise, Doppler probes also can be used to assess the status of digital arteries.

The Allen test (see Figure 7) is performed to ensure that normal arterial supply is present, with both ulnar and radial arteries contributing to the palmar arches and to ensure that there is col-

Figure 7. Technique for the Allen Test



This figure shows the proper technique to perform the Allen test. In 1, both arteries are compressed. In 2, the hand is clenched and relaxed several times to empty it of blood. In 3, a single artery is released and blood flow to the fingers evaluated. A normal result is obtained when each artery alone can provide adequate blood flow to the hand. This also can be modified for testing patency of digital arteries.
Reprinted with permission: Rosen P, Barkin R, Hockberger R, et. al, eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. St. Louis: Mosby; 1999:637.

lateral circulation between the superficial and deep arches. Some individuals will have incomplete palmar arch connections, resulting in a single artery providing dominant blood flow to the entire hand. Loss of this artery obviously will compromise much more of the hand than in a patient with normal blood supply from both arteries. As seen in Figure 7, first both radial and ulnar arteries are compressed in the wrist, and then the patient opens and closes the hand about 10-20 times to temporarily remove blood from the hand. The pressure over a single artery then is relieved. A normal result occurs when restoration of blood flow from a single artery reestablishes adequate blood flow to all fingers. An abnormal Allen test would be useful to identify a person with a single dominant arterial blood supply with injury to that vessel.

Table 1. What Not to Do with an Acute Hand

- Do not make predictions about the care a consultant will provide (i.e., re-implantation) or about the outcome of treatment the patient will receive from another physician.
  - The patient should receive the same message from all staff members caring for them (including nurses).
  - Do not give the patient conflicting information.
- Always perform a full sensory exam before giving local anesthesia.
- If possible, involve consultants early in complex cases to allow them the opportunity to participate if they desire.
  - This gives them "early warning" of a case that needs urgent attention from them and may accelerate care for the patient.
  - It also avoids later complaints that something was not done to their specification.
- Call the re-implantation team or begin transportation arrangements immediately upon presentation of patient with obvious need for re-implantation.
  - Do not wait for x-rays or any studies to be done.
  - Cool amputated part appropriately to minimize warm ischemia time.
- Minimize repeat examinations of a painful hand as much as possible.
- DO NOT blindly clamp vessels.
- Always close lacerations of the hand when discharging the patient to see the consultant in the office, except in cases of infection, bite wounds, or upon request by the consultant.
- Keep patients who may be OR candidates NPO while in the ED.

The Allen test can be modified for use on a single digit, as well, by compressing the radial and ulnar digital arteries at their bases instead.

Neurological Evaluation: Sensation. Nerve injuries are common and should be suspected any time a patient presents with an injury over the known location of a nerve. Even if a patient is unconscious, nerve function still can be tested. Loss of sweating can provide a clue to nerve injury and does not require the patient's cooperation to be evaluated. Another test used in the unconscious patient is the O'Riain's test. It is performed by immersing the involved hand in hot water for 10 minutes and observing the skin's reaction.[12] Normally innervated skin will wrinkle, while skin supplied by a severed nerve will not wrinkle. For a cooperative patient, first ask if he is experiencing any changes: differences in light touch, tingling, numbness, decreased (hypoesthesia) or increased sensation (hyperesthesia).

As mentioned previously, the radial nerve is a pure sensory nerve in the hand, while the ulnar and median nerves provide both motor and sensory input. As sensory input to the hand can vary in each individual, the integrity of each nerve should be tested where the least amount of dual innervation is likely. For the radial nerve, test the skin proximal to the first dorsal web space (radial side of the index metacarpal). For the ulnar nerve, test the volar tip of the little finger. For the median nerve, test the volar tip of the index finger. The most objective and accurate method to test for sensory nerve damage is with the two-point discrimination. Uninjured fingertips

should be able to distinguish two points 2-5 mm apart while, the normal palm threshold is 7-12 mm apart. Wider distances imply some loss of sensation.[13] Usually a bent paper clip is used to perform the test, but electrocardiogram (ECG) calipers may provide more accurate testing. The patient should be shown the process on an uninjured area first so that he is not confused about what is being done. When evaluating for a digital nerve injury, one should test the sides of a finger where dual innervation is less likely. Although a useful test in general, it is of limited value in children, patients with severe pain, mental status changes, or heavy calluses.

Neurological Evaluation: Motor Function. Although one will perform a complete motor exam on every patient, one can perform a simple screening test to quickly identify deficits. Have the patient extend his thumb fully (like hitchhiking). Next have the patient spread the fingers widely apart. Finally, ask him to move the tip of each finger and thumb (one at a time) in a circle around the tip of a pen. If the patient can perform all of these simple actions, then all three major nerves to the hand are intact.[12]

A complete motor evaluation is done by testing movement and strength at each joint of the hand. Range of motion of the wrist should be included. Lack of wrist extension ("wrist drop") implies radial nerve damage in the forearm. Loss of strength in the little and ring fingers ("claw hand") indicates ulnar nerve injury, and the same finding in the index and middle fingers implies median nerve damage. Laceration of the recurrent branch of the median nerve will cause loss of thumb opposition ("ape hand"). Test this by having the patient form an "O" with thumb and index finger. Ulnar nerve function also is required to perform this maneuver. Asking the patient to hold a single piece of paper tightly pinched with the thumb and index finger will perform the same action. An abnormal result is obtained if the examiner can easily pull the piece of paper away. Tendon lacerations can, at times, be confused initially with nerve injury as both can result in loss of movement. A simple tendon laceration will not result in changes in sensation unless there is a combined injury. Likewise, laceration of a single tendon only will affect the digit it terminates on. When one sees a single wound that produces loss of movement in multiple digits, a nerve injury is more likely, but a series of tendon lacerations can produce a similar result. Ultimately a patient with multiple deficits will not have his injuries truly defined outside the operating room (OR). For the emergency physician, the prime objective is not to miss an injury to a deep structure and refer the patient for consultation rather than to identify all the involved structures in every patient.

Range-of-motion tests rely on the presence of intact tendons. Tendon function can be tested simply with the following maneuvers. First, test the strength of digit extension against the examiner's finger. Remember from the anatomy section that the thumb, index, and little fingers have dual extensors and can maintain full strength with a significant tendon laceration. Likewise, the connections between the different branches of the extensor digitorum communis (juncturae tendinae) can provide some extension to a digit with complete EDC injury. The flexor tendons are tested by isolating flexion at the PIP joint (FDS) and the DIP joint (FDP). Both joints must be tested in all fingers to help rule out flexor tendon injury. It is important to realize that these range-of-motion and strength tests cannot by themselves rule out injury. A deficit can rule an injury in, but a normal result still requires sterile exploration in a bloodless field with adequate anesthesia to rule out an injury. Every time a laceration in the hand is repaired, it should be done only after a diligent search for injury to deep structures has been carried out.

Cleaning the Hand

Some controversy exists concerning the proper solution and technique to clean soft-tissue wounds.[14] It generally is accepted that cleaning solutions (hydrogen peroxide, iodine, hexachlorophene, etc.) should not be used directly in the wound. While useful in cleaning surrounding uninjured epidermis, they are damaging to exposed tissue in the wound. The axiom to remember is: "Only put into the wound what also would be used in the physician's eye." Use of large volumes of saline under moderate pressure is the most often recommended method for cleaning soft-tissue injuries. Using an 18-gauge needle or angiocath attached to a 20 cc or 30 cc syringe is the recommended approach for irrigation of hand wounds.

When to Get an X-ray

Radiographs of the hand are recommended in evaluation of any hand problem beyond minor trauma (i.e., superficial lacerations). It is important to remember that one must remain suspicious of injury to deep structures even in innocuous-appearing wounds. Although one may see evidence of fractures, etc., of the hand on wrist films and visa versa, separate hand and wrist series must be ordered to adequately characterize injuries of each area. The hand is positioned improperly on a wrist series for satisfactory imaging, and likewise, the wrist is not aligned correctly on a hand series. One should obtain posteroanterior (PA), true lateral, and oblique films in a standard hand series. The PA is useful but does not show fractures of the articular surface of the metacarpal (MC) head well. The lateral shows displacement of fractures and dislocations, and the oblique is helpful for assessing fractures of the base of the MCs and dislocations of MP and carpometacarpal (CMC) joints. If evaluating a thumb injury, separate PA and lateral views of the thumb are needed, as the thumb rests at 90° to the fingers and, thus, standard hand films will not give true PA or lateral views of the thumb. Stress views of a joint can be helpful to identify ligamentous injury of the thumb MP joint.

Plain films can identify many retained foreign bodies, but not all. Magnetic resonance imaging (MRI) and computed tomography (CT) may identify foreign bodies not seen on plain films, but these images of the hand are not effective screening tools for all patients as they can cost up to $1500. Ultrasound (US) is a much less expensive, and often readily available, alternative. US recently has been shown to be successful for location of wooden foreign bodies, which often are missed on plain films.[15] Another study evaluated 166 wood, glass, or metal foreign bodies specifically in the hand, and found US had a

specificity of 99% and sensitivity of 94%.[16] They concluded a combination of US and plain films should locate virtually all foreign bodies in the hand.

Management Tips—What Not to Do

Several principles should be kept in mind while treating a patient with an acute hand problem. First, do no harm. One of the most important mistakes to avoid is making predictions on the type of treatment that will be done or the outcome of the treatment. This especially is evident in the case of amputations, from small fingertip to multiple digits. A good rule is that only the physician who is rendering the final treatment (i.e., the consultant) should give the patient predictions on outcome and ultimate use of his hand. Loss of use of even part of a hand can be devastating in many ways. Giving patients unrealistic expectations at the outset, even if well-intentioned, can make it very traumatic for the patient and the consultant when the outcome does not live up to the initial prediction. In these situations it is very easy for the patient to become confused, hostile, and disappointed with conflicting information and lose confidence in the consultant's care. One should be very careful to make only general statements when treating amputations. In the case of less complex situations, such as an isolated tendon laceration, one can be comfortable providing general information on the situation (repair can be done any time in the next few days without affecting the end result; it can take six weeks to heal; and rehabilitation may be necessary afterwards, etc.). Nerve injuries involve long and sometimes complicated treatment, and it should be underscored to the patient that full recovery may not be possible even with the best care.

Several other management issues require emphasis. As previously stated, do not give local anesthesia to a hand injury without performing a full sensory exam first. The consultant may be called early in that case to give him the opportunity to perform his own sensory exam before anesthesia if he desires. This "preemptive strike" involves the consultant early in decision-making and avoids later complaints that something wasn't done to his preference. In the case where amputation(s) will be obvious candidates for re-implantation (proximal thumb, etc.), one should call the re-implantation team immediately upon presentation or begin arranging transfer for the patient. This will minimize ischemic time for the amputated part and maximize the chances of successful surgery. The care these patients require in the ED can be provided in parallel with the consultation, but ischemic time of the amputated part is critical; the arrival of the patient in the OR should not be delayed in any way by the ED. Repeated examinations of a painful hand should be avoided if possible. When there are several people in the ED who need to see the exam (i.e., a teaching situation), it is best to assemble everyone at one time so that the patient does not undergo unnecessary discomfort. As previously mentioned, blind clamping of bleeding arteries should be avoided. In most cases, bleeding can be controlled by direct pressure or inflation of a BP cuff proximal to the injury. Blind clamping is likely to accidentally injure adjacent nerves and tendons. Finally, in many cases a consultant may elect (appropriately) to see a patient in the office 24-48 hours after an injury. It is important to close lacerations with simple sutures before discharging the patient to the consultant. This helps prevent the complication of infection and growth of granulation tissue over tendons that can make primary repair impossible. Exceptions to this would be when the consultant specifically asks that the wound be left open, such as in the case of an infection, or injuries at very high risk for infection (bite wounds).

References

1. Antosia RE, Lyn E. The hand. In: Rosen P, et al, eds. *Emergency Medicine: Concepts and Clinical Practice*, 4th ed. St. Louis: Mosby; 1998:662-668.
2. Boles CA, Daniel WW, Adams BD, et al. Hand and wrist. *Radiol Clin North Am* 1995;33:319-354.
3. Overton DT, Uehara DT. Evaluation of the injured hand. *Emerg*

Med Clin North Am 1993;11:585-600.
4. Kohn MA. Hand injuries and infections. In: Markovichick VJ, Pons PT, eds. *Emergency Medicine Secrets*, 2nd ed. Philadelphia: Hanley & Belfus;1993:448-453.
5. Sorock GS, Lombardi DA, Hauser RB, et al. A case-crossover study of occupational traumatic hand injuries: Methods and initial findings. *Am J Ind Med* 2001;39:171-179.
6. Marty J, Porcher B, Autissier R. Hand injuries and occupational accidents. Statistics and prevention. *Ann Chir Main* 1983;2: 368-370.
7. Green DP, Rowland SA. Fractures and dislocations in the hand. In: Rockwood CA, Green DP, Bucholz RW, eds. *Rockwood and Green's Fractures in Adults*. Philadelphia: J.B. Lippincott; 1991; 441-561.
8. Grossman JA, Adams JP, Kunec J. Prophylactic antibiotics in simple hand lacerations. *JAMA* 1981;245:1055-1056.
9. Verdan CE. Primary and secondary repair of flexor and extensor tendon injuries. In: Flynn JE, ed. *Hand Surgery*, Philadelphia: Williams & Wilkins;1996:85.
10. Belliappa PP, Scheker LR. Functional anatomy of the hand. *Emerg Med Clin North Am* 1993;11:557-583.
11. Gellman H, Botte MJ, Shankwiler J, et al. Arterial patterns of the deep and superficial palmar arches. *Clin Orthop* 2001;383:41-46.
12. Stewart C, Winograd SM. Hand injuries: A step-by-step approach for clinical evaluation and definitive management. *Emerg Med Reports* 1997;18:223-234.
13. Sloan EP. Nerve injuries in the hand. *Emerg Med Clin North Am* 1993;11:651-670.
14. Anglen JO. Wound irrigation in musculoskeletal injury. *J Am Acad Orthop Surg* 2001;9:219-226.
15. Jacobson JA, Powell, A, Craig JG, et al. Wooden foreign bodies in soft tissue: Detection at US. *Radiology* 1998;206:45-48.
16. Bray PW, Mahoney JL, Campbell JP. Sensitivity and specificity of ultrasound in the diagnosis of foreign bodies in the hand. *J Hand Surg* 1995;20:661-666.

Physician CME Questions

91. Which of the following data should be obtained during evaluation of the acute hand?
    A. Hand dominance
    B. Occupation
    C. Time of injury
    D. Previous injuries or surgeries to the affected hand
    E. All of the above

92. Which of the following should be done in treatment of acute hand problems?
    A. Blind clamping to stop bleeding
    B. Application of local anesthesia before obtaining full sensory exam
    C. Repeated examination of a painful hand
    D. Making specific predictions concerning treatment to be provided by the consultant
    E. Notifying the hand surgeon as soon as patients with amputations present

93. Concerning hand anatomy, which of the following is true?
    A. There are two sets of extensors and one set of flexors for each digit.

Audio Conference Tackles HIPAA Privacy Concerns

The recently released final privacy rule under the Health Insurance Portability and Accountability Act (HIPAA) makes significant changes to the existing regulations. With the April 14, 2003, compliance deadline fast approaching, is your staff receiving the proper training?

The American Hospital Association says implementing HIPAA will require "sweeping operational changes" and will take "intense education of hospital workers and patients." To help you and your staff prepare, American Health Consultants offers HIPAA's Final Privacy Regulations: What You Must Know to Comply, an hour-long audio conference on Dec. 4, 2002, from 2:30-3:30 p.m., Eastern time. You'll learn detailed information on changes to the privacy rule, as well as practical methods to implement new procedures within your facility. Also learn how to successfully manage privacy issues with business associates, and how to spot and avoid costly HIPAA violations. Do you know what your enforcement priorities are? Do you need real-world examples? Our expert speakers, Debra Mikels and Chris Wierz, BSN, MBA, will help you understand your responsibilities and identify potential liabilities. All this will allow you to develop a HIPAA compliance strategy with a rationale behind it.

Mikels is corporate manager, confidentiality, for Partners Healthcare in Boston. The Partners system includes some of the largest and most respected facilities in the country, including Massachusetts General Hospital, Brigham and Women's Hospital, and Harvard Medical School. Mikels will provide the practical information and guidance you need to implement a comprehensive privacy policy in your organization.

Wierz is vice president of HIPAA and compliance initiatives for Houston-based Healthlink Inc., a health care consulting firm. She has worked with numerous facilities across the country to prepare them for HIPAA compliance, and now she shares many of her ideas with you.

The cost of the conference is $299, which includes free CE or CME for your entire staff, program handouts, and additional reading, a convenient 48-hour replay, and a conference CD. Don't miss out. Educate your entire facility for one low price.

For more information or to register for the HIPAA audio conference, please call American Health Consultants' customer service department at (800) 688-2421. When ordering, please refer to effort code: 65151.

B. The radial nerve is purely sensory in the hand.
C. The lumbrical muscles are not the primary MP flexors.
D. Tendon lacerations greater than 50% will show decreased range of motion.

94. The FDS can be severed completely and there still will be active flexion at both joints from the intact FDP.
A. True
B. False

95. Which of the following statements is true of extensor tendons?
A. The extensor tendons are rounded.
B. Extensor tendons are broad and flat.
C. They are more complicated than flexor tendons because there are two sets of extensor tendons and a pulley system.
D. There are six extensor tendons in four compartments on the dorsum of the hand.

96. Which of the following is true regarding the ulnar nerve?
A. It is critical to proper hand function.
B. Loss of ulnar nerve function results in loss of the pinching action of the index finger and thumb.
C. It provides sensation to the ulnar side of the hand, the little finger, and half of the ring finger.
D. It innervates the hypothenar muscles, seven interosseous muscles, lumbricals for the ring and little fingers, adductor pollicis, and both flexors to the ring and little fingers.
E. All of the above

97. Which of the following can be used directly in the wound for cleaning a hand injury?
A. Hydrogen pyroxide
B. Iodine
C. Saline
D. Hexachlorophene

98. Which of the following is true of obtaining x-rays for hand injuries?
A. X-rays are not recommended in evaluation of hand injuries beyond minor trauma.
B. Separate hand and wrist series must be ordered to adequately characterize injuries of each area.
C. Plain films can identify all foreign bodies as well as MRIs or CTs.
D. Ultrasound has not been found to be successful in showing the location of wooden foreign bodies.

99. Which statement is true regarding neurological evaluation for motor function in the hand?
A. Lack of wrist extension implies radial nerve damage in the forearm.
B. Loss of strength in the little and ring fingers indicates ulnar nerve injury.

United States Postal Service
Statement of Ownership, Management, and Circulation

1. Publication Title	2. Publication No.	3. Filing Date
Emergency Medicine Reports	0 7 4 6 - 2 5 0 6	10/14/02
4. Issue Frequency	5. Number of Issues Published Annually	6. Annual Subscription Price
Bi-weekly	26	$379.00

7. Complete Mailing Address of Known Office of Publication *(Not Printer) (Street, city, county, state, and ZIP+4)*
3525 Piedmont Road, Bldg. 6, Ste. 400, Atlanta, Fulton County, GA 30305
Contact Person: Willie Redmond
Telephone: 404/262-5448

8. Complete Mailing Address of Headquarters or General Business Office of Publisher *(Not Printer)*
3525 Piedmont Road, Bldg. 6, Ste. 400, Atlanta, GA 30305

9. Full Names and Complete Mailing Addresses of Publisher, Editor, and Managing Editor *(Do Not Leave Blank)*
Publisher *(Name and Complete Mailing Address)*
Brenda Mooney, 3525 Piedmont Road, Bldg. 6, Ste. 400, Atlanta, GA 30305
Editor *(Name and Complete Mailing Address)*
Shelly Morrow, same as above
Managing Editor *(Name and Complete Mailing Address)*
Valerie Loner, same as above

10. Owner *(Do not leave blank. If the publication is owned by a corporation, give the name and address of the corporation immediately followed by the names and addresses of all stockholders owning or holding 1 percent or more of the total amount of stock. If not owned by a corporation, give the names and addresses of the individual owners. If owned by a partnership or other unincorporated firm, give its name and address as well as those of each individual. If the publication is published by a nonprofit organization, give its name and address.)*

Full Name	Complete Mailing Address
American Health Consultants	3525 Piedmont Road, Bldg. 6, Ste 400 Atlanta, GA 30305

11. Known Bondholders, Mortgagees, and Other Security Holders Owning or Holding 1 Percent or More of Total Amount of Bonds, Mortgages, or Other Securities. If none, check box → ☐ None

Full Name	Complete Mailing Address
Medical Economics Data, Inc.	Five Paragon Drive Montvale, NJ 07645

12. Tax Status *(For completion by nonprofit organizations authorized to mail at nonprofit rates.) (Check one)*
The purpose, function, and nonprofit status of this organization and the exempt status for federal income tax purposes:
☐ Has Not Changed During Preceding 12 Months
☐ Has Changed During Preceding 12 Months *(Publisher must submit explanation of change with this statement)*

PS Form **3526**, September 1998 *See instructions on Reverse)*

13. Publication Name: Emergency Medicine Reports
14. Issue Date for Circulation Data Below: September 9 2002

15. Extent and Nature of Circulation			Average No. of Copies Each Issue During Preceding 12 Months	Actual No. Copies of Single Issue Published Nearest to Filing Date
a. Total No. Copies *(Net Press Run)*			7148	7300
b. Paid and/or Requested Circulation	(1)	Paid/Requested Outside-County Mail Subscriptions Stated on Form 3541. *(Include advertiser's proof and exchange copies)*	5680	5614
	(2)	Paid In-County Subscriptions *(Include advertiser's proof and exchange copies)*	22	17
	(3)	Sales Through Dealers and Carriers, Street Vendors, Counter Sales, and Other Non-USPS Paid Distribution	132	391
	(4)	Other Classes Mailed Through the USPS	0	12
c. Total Paid and/or Requested Circulation *(Sum of 15b(1) and 15b(2)*			5834	6034
d. Free Distribution by Mail *(Samples, Complimentary and Other Free)*	(1)	Outside-County as Stated on Form 3541	36	40
	(2)	In-County as Stated on Form 3541	1	1
	(3)	Other Classes Mailed Through the USPS	0	0
e. Free Distribution Outside the Mail *(Carriers or Other Means)*			19	0
f. Total Free Distribution *(Sum of 15d and 15e)*			56	41
g. Total Distribution *(Sum of 15c and 15f)*			5890	6075
h. Copies Not Distributed			1258	1225
i. Total *(Sum of 15g, and h.*			7148	7300
Percent Paid and/or Requested Circulation *(15c divided by 15g times 100)*			99	99

16. Publication of Statement of Ownership
Publication required. Will be printed in the October issue of this publication. ☐ Publication not required.

17. Signature and Title of Editor, Publisher, Business Manager, or Owner: Publisher — Date: 10/14/02
Brenda L. Mooney
I certify that all information furnished on this form is true and complete. I understand that anyone who furnishes false or misleading information on this form or who omits material or information requested on the form may be subject to criminal sanctions (including fines and imprisonment) and/or civil sanctions (including multiple damages and civil penalties).

Instructions to Publishers

1. Complete and file one copy of this form with your postmaster annually on or before October 1. Keep a copy of the completed form for your records.
2. In cases where the stockholder or security holder is a trustee, include in items 10 and 11 the name of the person or corporation for whom the trustee is acting. Also include the names and addresses of individuals who are stockholders who own or hold 1 percent or more of the total amount of bonds, mortgages, or other securities of the publishing corporation. In item 11, if none, check the box. Use blank sheets if more space is required.
3. Be sure to furnish all circulation information called for in item 15. Free circulation must be shown in items 15d, e, and f.
4. Item 15h., Copies not Distributed, must include (1) newsstand copies originally stated on Form 3541, and returned to the publisher, (2) estimated returns from news agents, and (3), copies for office use, leftovers, spoiled, and all other copies not distributed.
5. If the publication had Periodicals authorization as a general or requester publication, this Statement of Ownership, Management, and Circulation must be published; it must be printed in any issue in October or if the publication is not published during October, the first issue printed after October.
5. In item 16, indicate date of the issue in which this Statement of Ownership will be published.
6. Item 17 must be signed.

Failure to file or publish a statement of ownership may lead to suspension of second-class authorization.

PS Form **3526**, September 1999 *(Reverse)*

C. Loss of strength in the index and middle fingers implies median nerve damage.
D. Loss of thumb opposition can occur when the recurrent branch of the median nerve is lacerated.
E. All of the above

100. Lacerations should be closed with simple sutures before discharge to the consultant, except if the consultant requests the wound be left open, in the case of infection, or in wounds at high risk of infection, such as bite wounds.
A. True
B. False

Emergency Medicine Reports

CME Objectives

To help physicians:

- quickly recognize or increase index of suspicion for specific conditions;
- understand the epidemiology, etiology, pathophysiology, and clinical features of the entity discussed;
- be educated about how to correctly perform necessary diagnostic tests;
- take a meaningful patient history that will reveal the most important details about the particular medical problem discussed;
- apply state-of-the-art therapeutic techniques (including the implications of pharmaceutical therapy discussed) to patients with the particular medical problems discussed;
- understand the differential diagnosis of the entity discussed;
- understand both likely and rare complications that may occur;
- and provide patients with any necessary discharge instructions.

In Future Issues:

Hand Emergencies, Part II

Smallpox Vaccinations Imminent for Hospitals

Know the consequences for your facility

The Atlanta-based Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP) recently approved a plan that calls for smallpox immunization of 510,000 health care workers.

The plan suggests that all hospitals should designate a "smallpox care team" that will be immunized prior to any release of the virus. The committee recommends that the team include a minimum of 40 health care workers per hospital, with some hospitals vaccinating 100 or more, including emergency department physicians and nurses, infection control professionals, intensive care unit nurses, infectious disease consultants, radiology technicians, respiratory therapists, engineers, security, and housekeeping staff.

To help you prepare for sweeping procedural changes, American Health Consultants offers Imminent Smallpox Vaccinations in Hospitals: Consequences for You and Your Facility, a 90-minute audio conference Wednesday, Dec. 11, from 2-3:30 p.m., EST. This session is designed to help you and your staff answer serious questions and prepare your facility for the inevitable. How will being vaccinated affect you? How do you protect yourself, patients, and family? What are the logistics of implementing a smallpox care team? How do you deal with vulnerable populations? How do you minimize side effects?

This panel discussion will be led by William Schaffner, MD, chairman of the department of preventive medicine at Vanderbilt University Medical Center in Nashville, TN. A veteran, award-winning epidemiologist who has seen actual cases of smallpox and currently oversees a volunteer smallpox vaccine study at Vanderbilt, Schaffner began his distinguished medical career as a medical detective in the CDC's Epidemic Intelligence Service. He also is a liaison member of ACIP. Schaffner and an expert panel of emergency and infection control professionals will help you prepare for this critical task.

The cost of the program is $299, which includes 1.5 hours of free CE, CME, ACEP Category I, and critical care credits. You can educate your entire facility for one low fee.

The facility fee also includes handout material, additional reading and references, as well as a compact disc recording of the program for continued reference and staff education. For more information, or to register, call customer service at (800) 688-2421. When ordering, please refer to the effort code: 65341.

AMERICAN HEALTH CONSULTANTS®

Evidence-Based Medicine for the ED

Trauma Reports

Vol. 3, No. 6

Supplement to *Emergency Medicine Reports*, *Pediatric Emergency Medicine Reports*, *ED Management*, and *Emergency Medicine Alert*

Nov./Dec. 2002

One Year Later: Emergency Department Response to Biological Terrorism

Part II: Smallpox, Viral Hemorrhagic Fevers, Tularemia, and Botulinum Toxins

Author: **Kevin Coonan, MD,** Department of Emergency Medicine, Madigan Army Medical Center, Fort Lewis, WA.

Peer Reviewer: **Steven Winograd, MD, FACEP,** Attending Physician, Department of Emergency Medicine, Jeannette District Memorial Hospital, Jeannette, PA; St. Clair Memorial Hospital; University of Pittsburgh Medical Center; Pittsburgh, PA,

The threat of bioterrorism continues to loom over the United States with emergency departments likely to be the front lines. In the second article of this two-part series, the author updates the emergency department (ED) physician on the current status of smallpox, viral hemmorhagic fevers, tularemia, and botulism as both disease entities and weapons of bioterrorism.

—The Editor

Smallpox

Clinical Features. Few diseases have rivaled smallpox as a cause of human suffering and death, with epidemics of smallpox surpassing other diseases such as plague, cholera, and yellow fever as instruments of morbidity and mortality.[1] It is ironic that the possibility of an outbreak is more feasible after this disease has not been seen in the last quarter-century and vaccination programs were halted in the wake of this accomplishment.[2-4] Known repositories of variola are limited to the two sites specified by the World Health Organization (WHO): the Centers for Disease Control and Prevention (CDC) in Atlanta and VECTOR in Novosibirsk, Russia. The former Soviet Union had created weapon forms of variola in ton quantities. While the stockpiles of smallpox reportedly were destroyed, the accounting of such is incomplete and the true disposition is uncertain.[5] In addition, other nations strongly are suspected of maintaining hidden stocks as part of clandestine biological weapons programs.[6,7]

Smallpox is extremely contagious. In one of the last outbreaks in Europe, a single index patient infected 11 others, who subsequently infected 175 others, resulting in 35 deaths. Due to the delay in clinical diagnosis, some 10,000 contacts of patients had to be quarantined and 20 million were vaccinated.[8] In conditions of low temperature and low humidity, aerosolized variola is very stable, and has resulted in widespread, hospital-based epidemics. The predominant method of transmission is by respiratory droplet requiring face-to-face (within 2 meters) contact, although patients with cough frequently generate infectious aerosols that may result in airborne spread. Infected bed linens and other fomites also have resulted in a small number of outbreaks. In previous epidemics it was common to see 10-20 secondary cases from each infected patient, eventually resulting in one-third of all contacts becoming infected.[9,10] Infectivity is maximal during the first week of rash, and is increased markedly in patients who manifest a cough.[6]

The case fatality rates are strain-dependent, with fewer than 1% in immunologically naïve patients infected with the variola minor strain, but 30% of unimmunized and 3% of vaccinated patients infected with variola major. Soviet scientists had developed strains with considerably higher virulence and transmissibility. This, coupled with the large inoculum expected from an intentional aerosol release, likely would result in much higher fatality rates.[11]

Following a 10- to 14-day incubation period, patients with smallpox present with acute onset of fever, prostration, malaise, myalgias, rigors, vomiting, backache, and cephalgia.[10] Patients appear toxic, and some fair-skinned patients will exhibit an erythematous exanthem. Acute delirium is seen in 15% of patients. After 2-3 days, the pathognomic rash begins as an enanthem on the oropharynx, and within 1-2 days develops on the face, forearms, and hands. It then spreads to the trunk and lower extremities. The lesions begin as macules and display synchronous development into deeply rooted papules. These lesions subsequently evolve into vesicles and tense, often umbilicated, pustules.[12] Approximately 8-9 days after eruption, the pustules involute and form scabs, eventually crusting on days 14-16. The crusting of the lesions is associated with resolution of fever. A week later, the crusts separate, leaving hypopigmented scars, particularly on the face.[6] Lesions may be so extensive as to appear confluent. Cough and bronchitis commonly are associated with infection, but pulmonary consolidation is unusual except in fatal cases. Secondary bacterial infections are rare. Monkeypox is identical in presentation, except that lymphadenopathy is more common and mortality is only 10-15%.[13]

Variola minor shows a similar progression of symptoms with less toxicity and often smaller lesions. Both show the typical progression starting with the face and lower arms, with fewer lesions on the abdomen, and with all lesions in adjacent anatomic areas at the same stage of development.[14] One-fifth of variola major resulted in atypical presentations. Modified smallpox often was seen in those with prior vaccination, with sparse, short-lived skin lesions and infrequent toxicity. Even those with recent immunization were susceptible to a brief upper respiratory infection after exposure. Flat-type smallpox has been reported in 2-5% of cases, with severe systemic toxicity associated with slow development of flat, soft, velvety skin lesions; it usually is fatal (95% in unvaccinated patients, 66% in vaccinated). Hemorrhagic smallpox, seen most often in pregnant women, shows a rapid progression, with development of mucosal bleeding, petechiae, and ecchymoses prior to death.[12,14] Asymptomatic infections likely are more common than previously appreciated, and virus may be recovered from the oropharynx of such individuals. The potential transmission from these asymptomatic carriers is not known, but probably is limited.[9,14]

Diagnosis. Historically, experienced clinicians in endemic areas reliably could diagnose smallpox based on clinical features. However, in nonendemic areas, variola minor frequently was confused with varicella. However, varicella lesions are more superficial, evolve in a variety of stages over a given anatomic region, spare the soles and palms, and are more prominent on the trunk.[8] Other exanthems and pustular dermatosis that were less frequently confused with smallpox lesions include erythema multiforme with bullae, contact dermatitis, and impetigo.[6,10]

Treatment. Treatment largely is supportive and symptomatic. Strict isolation to reduce secondary transmission is essential starting with onset of rash until all scabs have separated. Anyone exposed to a patient in this time period must be vaccinated and quarantined for 17 days.

Antiviral therapy historically has not been useful. Both cidofovir and ribavirin inhibit variola in vitro, and both had significant but lesser activity against monkeypox and vaccinia.[15] Cidofovir, currently licensed in the United States for treatment of cytomegalovirus (CMV) retinitis at a dose of 5 mg/kg, is protective in a mouse cowpox model at a 20-fold higher dose.[16] Cidofovir only is available as an intravenous formulation, and must be administered with concomitant hydration and probenecid to reduce the risk of nephrotoxicity.[17] There are no in vivo studies of ribavirin for poxvirus infections. Other proposed antiviral therapies are undergoing study.[18,19]

Vaccination is effective in preventing infection or attenuating disease. It is possible that EDs will assist in a public health disaster by providing vaccination, and it is certain that any vaccine-related complications would require ED intervention.

Trauma Reports™ (ISSN 1531-1082) is published bimonthly by American Health Consultants, 3525 Piedmont Road, N.E., Six Piedmont Center, Suite 400, Atlanta, GA 30305. Telephone: (800) 688-2421 or (404) 262-7436.

Vice President/Group Publisher: Brenda Mooney
Editorial Group Head: Valerie Loner
Managing Editor: Allison Mechem
Marketing Manager: Schandale Kornegay

Periodicals postage paid at Atlanta, GA.
(GST registration number R128870672.)

POSTMASTER: Send address changes to ***Trauma Reports***, P.O. Box 740059, Atlanta, GA 30374.

Accreditation

Trauma Reports™ continuing education materials are sponsored and supervised by American Health Consultants. American Health Consultants designates this continuing education activity for up to 2.5 hours in Category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

This CME activity was planned and produced in accordance with the ACCME Essentials.

American Health Consultants (AHC) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

THOMSON™
AMERICAN HEALTH CONSULTANTS

Subscriber Information

Customer Service: 1-800-688-2421

Customer Service E-Mail: customerservice@ahcpub.com
Editorial E-Mail: allison.mechem@ahcpub.com

World Wide Web page: http://www.ahcpub.com

Subscription Prices

FREE to subscribers of *Emergency Medicine Reports, Pediatric Emergency Medicine Reports, Emergency Medicine Alert*, and *ED Management.*

For nonsubscribers, the price is $199.

U.S. possessions and Canada, add $30 plus applicable GST. Other international orders, add $30.

Back issues: $66. One to nine additional copies, $159 each; 10-20 additional copies, $119 each.

For Customer Service,
Please call our customer service department at **(800) 688-2421.** For editorial questions or comments, please contact **Allison Mechem**, Managing Editor, at allison.mechem@ahcpub.com.

Financial Disclosure

In order to reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, Drs. Dietrich (editor in chief), Bowman, Diebel, Falcone, Hanlon, Jones, Mahadevan, Perkin, Santanello, Savitsky, and Stafford (editorial board members), and Winograd (peer reviewer) report no relationships with companies related to the field of study covered by this CME program. Dr. Coonan (author) is a former infectious disease officer at USAMRIID and does ongoing consulting work.

Vaccination within five years prior to or within 2-3 days after natural exposure provides almost complete protection.[12] Revaccination is associated with prolonged immunity. To add a margin of safety, the WHO recommends revaccination if exposure occurs more than three years after vaccination. Vaccination 4-5 days after exposure attenuated natural disease and reduced death rates.[8]

Vaccinia immune globulin (VIG) has limited potential as a post-exposure prophylactic agent if given within a week of exposure in conjunction with vaccination.[10] It is given at a dose of 0.6 cc/kg, often requiring multiple intramuscular injections (as the volume for a typical adult is 42 cc), and can be repeated in 2-3 days if symptoms progress. Supplies are available through the CDC. It was derived for treatment of complications of vaccination, including eczema vaccinatum and some cases of progressive vaccinia. It also can be used in cases of severe generalized vaccinia. It is not effective in post-vaccination encephalitis, and is of no benefit in treatment of smallpox.[20]

Following successful dermal inoculation with the vaccine (referred to as a "take"), a papule forms after 4-5 days. This often intensely pruritic papule evolves over 2-3 days to an umbilicated vesicle or pustule, with surrounding erythema and induration peaking a week after initial appearance. Regional lymphadenopathy and mild systemic symptoms with fever are common. The pustule frequently ruptures prior to forming a scab, which separates with scarring two weeks later. The vaccination site must be covered with a non-occlusive dressing (e.g., a gauze pad) until the scab separates, and strict hand washing after contact with any drainage is essential to limit the inadvertent inoculation of additional sites or persons.[10,12,20] Occlusive dressings result in maceration and extensive local infection and should be avoided. Systemic antihistamines and non-narcotic analgesics often are useful for patient comfort. Common adverse effects which require only symptomatic treatment include nonspecific erythematous or urticarial eruptions, which may be confused with generalized vaccinia, as well as erythema multiforme.[20] Generalized vaccinia results in a vesicular eruption 7-9 days after vaccination, often accompanied by fever. The eruption usually is self-limited, requiring therapy only in immunocompromised patients.[10]

While most vaccinees experience mild morbidity that rarely interferes with activity, serious complications occur in 0.13% of primary vaccinations and an order of magnitude less often in revaccination.[21] The most common complication, accounting for over half of the serious adverse effects, is accidental inoculation of a site distant to the inoculation. Infection of the face, genitals, and rectum are common, but usually self-limited. More concerning are ocular infections, which account for one-fifth of accidental infections, which can result in corneal injury with permanent defects. One-fifth of accidental ocular infections occurred due to contact with a vaccinated person.[22] Ocular infection responds reasonably well to VIG and topical idoxuridine (one drop in affected eye q1h while awake, q2h while asleep).[10] However, if keratitis is established, there is an increased risk of corneal scarring with use of VIG, and its use is contraindicated.[20]

Eczema vaccinatum results in extensive or even generalized vaccinia infection in patients with eczema or other exfoliative skin disorders and, perhaps, burn victims. The disease usually is self-limited, but as many as one in 10 cases can be fatal.[10] It occurs independent of the current degree of eczema. Treatment with VIG is indicated and usually effective. If vaccination is essential, it can be done with concomitant administration of VIG.[20] VIG also is indicated in cases of vaccinia necrosum, a progressive vaccinia infection with extensive local destruction and metastatic lesions. Progressive vaccinia occurs only in patients with deficiencies in cell-mediated immunity and is fatal in three-quarters of cases.[10] Post-vaccination encephalitis complicates 12 per 1 million primary vaccinations, and two per 1 million revaccinations. VIG is ineffective and is not indicated.[20]

Routine contraindications to vaccination include immunosuppression, eczema, pregnancy, household contact with individuals with contraindications, or in children. Prior experience with vaccination showed very rare congenital infections, usually fatal, after primary vaccination of pregnant mothers. Prior to smallpox eradication, vaccination routinely was done in children, and in the face of exposure, this should not deter vaccination. In the face of a documented exposure to smallpox, it may be necessary to vaccinate even those with contraindications with concomitant VIG administration.[11,20]

Viral Hemorrhagic Fevers

Clinical Features. The viral hemorrhagic fevers (VHF) are prominent emerging infectious diseases. A variety of enveloped RNA-containing viruses are capable of causing severe illness marked by fever, shock, multi-organ failure, and hemorrhagic diathesis of varying severity. Recent outbreaks of Ebola hemorrhagic fever (EHF) in West Africa and Crimean-Congo hemorrhagic fever (CCHF) in Pakistan have highlighted the high mortality and potential for person-to-person transmission.[23] Increasing concern about the public health impact of VHF and potential to extend beyond traditional geographic boundaries is heightened by the potential for these highly infectious viruses to be used as terrorist weapons.[24,25] While technically difficult to produce in quantities similar to the former Soviet Union, small-scale production suitable for terrorist use can be accomplished in a typical two-car garage with minimal modifications.[26]

The filoviruses, Ebola and Marburg, have been responsible for severe explosive outbreaks and sporadic nosocomial cases. A well-documented, large outbreak occurred in Zaire in 1995, with 316 cases and an 80% fatality rate.[27-30] One-quarter of those infected in the Kikwit, Zaire, outbreak were health care workers.

The arenaviral hemorrhagic fevers are caused by Lassa fever virus, from Africa, and the Tacaribe complex of South American viruses: Machupo (Bolivian), Junin (Argentinean), Sabia (Brazilian), Guanarito (Venezuelan), and the recently described North American Whitewater Arroyo virus.[31-33] Human infection results from inhalation of infected rodent waste products, and may be transmitted person-to-person. Lassa fever is a substantial public health problem in West Africa, and accounts for one-quarter of febrile hospital admissions and deaths.[34]

CCHF has a wide endemic area, with sporadic tick-borne outbreaks and frequent hospital-centered outbreaks, marked by a

high incidence of fatal infections in health care providers.[33,35]

The filoviruses are associated with high-level viremia and widespread cytopathic effects without evidence of concomitant immunologic effect. Thrombocytopenia and lymphopenia with marked lymphoid depletion of bone marrow, spleen, liver, and peripheral lymph nodes only partially account for the immunosuppression.[36,37] While evidence of a consumptive coagulopathy occurs in the majority of patients, it is likely that direct viral destruction of endothelium and direct viral toxic effects are substantial contributors.[38,39] Hepatopathy without icterus usually is evident with elevations of aspartate aminotransferase (AST) greater than alanine aminotransferase (ALT).[40,41] Myocarditis and encephalitis appear common, but frequency depends on strain-specific features.[42] The virus survives in immunological privileged sites, such as the anterior chamber of the eye or the testes, which likely accounts for the delayed clinical features and protracted excretion of infectious virus in semen in survivors.[43-45] Similarly, the arenaviruses result in substantial thrombocytopenia, lymphopenia, and necrosis of liver, spleen, and adrenals without associated inflammatory response.[46]

All are highly infectious by aerosol in very low titers; perhaps as little as a single virion is infectious. All but yellow fever have been associated with person-to-person transmission and nosocomial epidemics. In the Kikwit Ebola outbreak, one-third of the physicians and one-tenth of the nurses contracted Ebola. The filoviruses are found in large amounts in and on skin. Physical contact with intact skin appears to be sufficient for transmission.[47] It appears, based on a small number of animal and epidemiological observations, that a minority of patients can generate infectious aerosols.[43,48-50] Argentine hemorrhagic fever (AHF) and Bolivian hemorrhagic fever (BHF) appear less transmissible, with occasional person-to-person spread, but may be secreted in semen after recovery, resulting in infection in intimate partners.[51] Guidelines for management of these patients are based on the infrequent generation of highly infectious aerosols, and call for strict respiratory and mucosal protection, negative airflow precautions, and isolation and decontamination of all bodily fluids.[24,35,52,53]

All agents of VHF present as a similar, non-specific febrile illness. Myalgias, malaise, prostration, and headache are nearly universal. Orthostatic symptoms and relative bradycardia appear common. The arenaviruses typically present with insidious onset. Common physical findings include evidence of diffuse capillary leak with hypovolemia, conjunctival injection, flushing, and petechia.[42,54-57]

Significant hemorrhage is present inconsistently and the absence of a bleeding diathesis should not dissuade the clinician from considering the possibility.[41] Minor bleeding—typically gingival, gastrointestinal, or oozing from vascular puncture sites—is seen in approximately 13% of AHF infections (Junin virus); 50% of VHF cases (Guanarito virus) and 40% of Ebola (Zaire strain) infections.[54,55]

Ebola typically presents with significant gastrointestinal (GI) symptoms, with non-bloody diarrhea present in more than 80% of patients and vomiting in 60%. Sore throat is a symptom in two-thirds of patients. Chest pain was a prominent feature in the Ebola-Sudan (EBO-S) outbreaks, but was not prominent in patients afflicted with Ebola-Zaire (EBO-Z) or Marburg disease.[58] A non-pruritic morbilliform or macular rash frequently is seen in fair-skinned individuals. The disease progresses in a biphasic manner with apparent recovery after the first week. A minority will have mild disease and continue to convalesce gradually over the next six weeks with frequent sequelae, while the majority will develop the hemorrhagic signs, tachypnea, hiccoughs, encephalopathy, normothermia, and oliguria that precede death.[59]

AHF, the most common and best characterized of the South American arenaviruses, typically presents 6-14 days after exposure, but the incubation period may range from four to 21 days. Onset is insidious, with fevers, chills, anorexia, myalgias, and malaise progressing over several days to prostration, tremor, cephalgia, abdominal pain, photophobia, and GI motility disturbance. Sore throat, nasal congestion, and cough are distinctly absent, and are helpful in limiting the differential diagnosis. Examination may reveal flushing of the face and upper torso with edema and hyperemia of the conjunctiva, gingiva, and oropharynx. Petechiae of the soft palate and axilla are common, along with small palatal vesicles and cervical lymphadenopathy. Patients often develop neurologic disease within a week of presentation, with a wide range of central nervous system (CNS) dysfunction, including ataxia, decreased deep tendon reflexes, and hyperesthesia. Three-quarters of patients will improve over the second week of illness, with the others manifesting bleeding, progression of CNS disease, shock, and secondary bacterial infections, particularly pneumonias. Convalescence is protracted, and up to 10% of antihemophilic factor A (AHF) patients treated with immune plasma developed a late onset self-limiting neurologic syndrome. Mortality ranges from 15-30%, with coma, severe bleeding, seizures, and oliguria portending poorer outcome. Treatment with immune plasma or ribavirin has reduced this to approximately 1%.[51,60]

Lassa fever differs only slightly in presentation from the South American arenaviruses, with less neurologic involvement, less prominent bleeding diathesis, and inconsistent thrombocytopenia or leukopenia.[61-63] Recovery typically takes 10 days. A minority develop edema, encephalopathy, tachypnea, hypotension, and bleeding manifestations portending a poor outcome.[64] Higher case fatality rates occur in pregnant women and fetal loss is universal.[65] Lymphopenia may be seen, but white blood cells may be unaffected or may reflect a neutrophilia, particularly in severe cases.[61,66] Disseminated intravascular coagulation (DIC) is not associated with Lassa fever. An elevated AST (> 150 U/L) is associated with worse prognosis and is an indication for initiation of ribavirin therapy.[34,67,68]

Most VHFs present with nondiagnostic features in a seriously ill-appearing patient with multiple organ involvement similar to other biowarfare (BW) agents and endemic diseases of the tropics. Misdiagnoses have been common. Similar presentations are shared by a variety of tropical viral agents, such as yellow fever, dengue, and the Hantaviruses responsible for hemorrhagic fever with renal syndrome, and Rift Valley fever, all of which have limited BW potential and can present with hemorrhagic manifesta-

tions. Other tropical diseases include malaria and leptospirosis, which have been seen in conjunction with Ebola outbreaks in the past, and may confound the diagnosis and treatment of both. Other diseases considered in the differential diagnosis include typhoid fever, borreliosis, septicemic plague, typhus, dysentery, acute African trypanosomiasis, fulminant meningococcemia, or other causes of sepsis with DIC.[33,69]

Diagnosis. Any evidence of a bleeding diathesis should result in isolation and aggressive diagnostic testing, to include attempts at viral isolation at one of the reference laboratories with biocontainment capabilities.[33,52,70] Lymphopenia and thrombocytopenia commonly are seen in all VHF syndromes and are ubiquitous in arenaviral disease, and a platelet count of fewer than 100,000 or WBC fewer than 4500 is 100% sensitive.[54] Almost all patients will have laboratory evidence of a consumptive coagulopathy, but rarely full-blown DIC may be present. Similarly, all patients with arenaviral disease display proteinuria, which also is common in the other VHFs.[71-73]

Laboratory diagnosis of VHF is difficult, and even routine blood tests (e.g., CBC and chemistries) pose severe hazards to laboratory workers. If VHF is in the differential, the laboratory must be warned, and physiochemical viral inactivation must be employed.[52,74,75]

Viral culture often is essential to establish the diagnosis. Most patients have intense viremia at presentation and viral cultures can yield a specific diagnosis in 3-10 days. This must only be attempted under BSL-4 conditions by experienced technicians. Samples should be sent to a reference laboratory *(See Insert)*, after contacting the laboratory to arrange shipping and packaging details.

Rapid diagnostic testing is available for all the VHF agents, and antigen detection tests show remarkable sensitivity in acute disease. These tests are available through the reference laboratory system, and some may be available at local level B or C laboratories, as they do not require biocontainment after specimen inactivation.

Treatment. All VHF syndromes require barrier nursing and intensive supportive care, which has been shown to improve outcomes. Invasive procedures and IM injections should be avoided. No therapy available, including interferon, antibody preparations, or currently marketed antiviral drugs, is effective against the filoviruses.[76-79] Intensive efforts at developing new drugs have been promising.[80,81] Antibody preparations, chiefly in the form of serum or plasma from convalescent patients, reduces mortality of the South American arenaviruses, but is no longer available in the United States, and may be associated with late-onset neurological disease.[82-84] Uterine evacuation, in pregnant patients, improves survival in Lassa Fever and is indicated as fetal loss is ubiquitous.[65]

Ribavirin inhibits the arenaviruses, RVF, and CCHF.[79,85] Ribavirin is well tolerated with mild reversible hemolytic anemia as the only consistent adverse effect.[17,52,85] The initial dose is 30 mg/kg IV given over one-half hour in saline or 2 g orally. Intravenous ribavirin is available through the reference centers listed in the Insert. Survival benefit has been shown in large studies with the arenaviruses. Although experience with ribavirin in RVF and CCHF is limited, it is recommended.[68,79,83,86-90]

Tularemia

Clinical Features. Tularemia is a zoonotic infection that in many ways resembles brucellosis and plague. Sporadic outbreaks in the United States continue to occur, with frequent misdiagnosis.[91] While hospital microbiology laboratory acquired infections are common, person-to-person transmission has not been described.[92,93] Aerosolized *F. tularensis* is highly infectious, with 10-50 organisms required to establish infection in healthy adult humans.[94]

Tularemia's incubation period typically is 3-6 days, dependent on route and dose of inoculation, but may range from 1 to 21 days.[95,96] As many as six different clinical forms of tularemia have been described, depending on the site of local infection and degree of dissemination. Common presentations include local ulceration and lymphadenopathy (ulceroglandular), lymphadenitis (glandular), conjunctivitis with lymphadenopathy (oculoglandular), ulcerative or exudative pharyngitis, and pneumonia.[93,97] Ingestion of contaminated water commonly results in pharyngitis, abdominal pain, and fever. Regardless of the presenting form, systemic symptoms of asthenia, malaise, fatigue, myalgias, low back pain, headache, chills, and fever usually are seen.[92]

In approximately one-quarter of all cases, systemic dissemination may occur following one of the localized forms or in the absence of other signs, resulting in the typhoidal presentation.[94] Diagnostic considerations include typhoid fever, typhus, brucellosis, Legionella infection, Q fever, malaria, disseminated mycobacterial or fungal infections, rickettsiosis, endocarditis, primary HIV infection, toxic-shock syndrome, and other causes of sepsis. Mortality approaches 33% in typhoidal cases, in contrast to only 4% in ulceroglandular disease.[94,95]

Primary pulmonary tularemia, the chief form expected following aerosolization, presents with abrupt onset of high fevers, rigors, dyspnea, nonproductive cough, pleuritic chest pain, and diaphoresis. It may result in systemic disease without localizing pulmonary disease or progress to a fulminant, fatal pneumonia.[92] The pulmonary form is indistinguishable from other common causes of community-acquired, zoonotic, fungal, and tubercular pneumonia. A pulse-temperature discrepancy occurs in up to 42%.[95] Production of purulent sputum or hemoptysis are seen in a minority.[98,99] Pneumonia also may complicate dissemination from localized infection and present with a more indolent course, chronic fevers, cachexia, fatigue, and lymphatic suppuration. It is seen in 83% of typhoidal cases.[95]

Pulmonary findings are nonspecific, with rales and friction rubs most often described. Radiographic findings may mimic tuberculosis, with multiple granulomatous lesions, hilar adenopathy and effusions, or may present with typical pneumonic findings such as subsegmental or lobar consolidation.[100] The triad of oval opacities, hilar adenopathy, and pleural effusions are strongly suggestive of tularemia, but are seen only in a minority of cases.[99]

Exam may show evidence of simultaneous extrapulmonary inoculation, most typically pharyngitis. The ulcerative and exudative pharyngitis commonly is confused with infectious mononucleosis, adenoviral tonsillopharyngitis, or streptococcal pharyngitis. It may become membranous, similar in appearance to diphtheria.[101,102]

Localized infection resulting in ulceroglandular or oculoglandular tularemia remains the most common natural presentation. Localized disease may occur even with aerosol exposure.[92] The majority develop an abrupt fever, with variable complaints of chills, malaise, fatigue, cough, and headache. Fever, as well as the other systemic symptoms, may remit and recur for weeks to months.[93] Following cutaneous inoculation, patients develop a small, painful, papule which rapidly necroses and ulcerates. Lymphadenopathy may occur as an isolated finding, or may persist well beyond the acute febrile illness.[95] Ocular manifestations are analogous, with corneal or conjunctival ulcerations, conjunctivitis and anterior chamber inflammation, or even frank hypopyon.[103] Meningitis is an exceedingly rare manifestation.

The ulceroglandular form of tularemia may be mistaken for the cutaneous form of anthrax, sporotrichosis, and *Mycobacterium marinum*. However, the papule and ulcer of tularemia are painful with local adenitis, in sharp distinction to that of the more edematous anthrax, which has minimal discomfort.[99] Other considerations include pyogenic infections, cat-scratch disease, syphilis, chancroid, and herpetic whitlow.

In addition to the pathognomonic skin lesions, a wide range of disseminated dermatological manifestations has been described, and may occur in up to one-third of patients within the first two weeks of illness, including diffuse maculopapular and vesiculopapular eruptions, erythema multiforme, acneiform lesions, urticaria, and, most commonly, erythema nodosum.[14,104]

Diagnosis. Routine laboratory studies are nonspecific. Lymphocytosis occasionally is seen, but the lymphocyte count is most often within normal limits. Up to one in four may show microscopic pyuria, which may lead to misdiagnosis of pyelonephritis. Minimal transaminase and lactate dehydrogenase elevations reflect hepatic infection and infrequently patients may develop rhabdomyolysis with the associated elevation of creatine phosphokinase (CPK).[95]

Francisella tularensis is difficult and dangerous to cultivate in hospital microbiology laboratories.[105] The organism is not typically seen on Gram stain of clinical specimens, but may be cultured from blood, lymph node aspirate, pharyngeal swabs, sputum, and cutaneous or corneal ulcers. Modern automated blood culture systems detect *F. tularensis* in at least 60% of bacteremic cases, but misidentification is common.[106,107]

Due to the difficulties with culture, diagnosis typically is accomplished via serology.[108] Cross-reactivity to Brucella and Legionella is seen. Polymerase chain reaction (PCR) is emerging as a valuable tool, with rapid return of accurate results without the risk of laboratory acquired infection.[109-111] Additional diagnostic assistance can be obtained through the Division of Vector-Borne Infectious Disease, CDC, Ft. Collins, CO (dvbid@cdc.gov). *(See Insert.)*

Treatment. Untreated, most patients have a prolonged debilitating febrile illness lasting months. Antibiotic treatment may result in a rapid improvement, but a substantial number of patients have a suboptimal response, particularly if ineffective antibiotic therapy is used, therapy is abbreviated, or if there is a delay in initiation of treatment.[92,112] A Jarisch-Herxheimer-like reaction may be seen with initiation of antibiotic therapy. Streptomycin or gentamycin for 10-14 days is the standard treatment regimen, although longer or repeated courses may be required.[9,92,113,114] Streptomycin-resistant organisms were engineered and investigated by both the United States and Soviet programs.[92] Ceftriaxone has an unacceptably high treatment failure rate and should not be used.[115] Doxycycline and chloramphenicol have been used extensively, but have higher treatment failure and relapse rates than the aminoglycosides, particularly in those with immunocompromise or chronic systemic disease.[116,117] A minimum of 14 days of treatment is recommended.[92] The addition of chloramphenicol to an aminoglycoside is recommended in the rare cases of meningitis.[118] Fluoroquinolones, principally ciprofloxacin, have been used in a limited number of cases, appear to be very effective, and are a reasonable first-line alternative to the aminoglycosides.[49,116] A 10-day course is recommended.[92]

Limited studies in humans demonstrate that a two-week course of a tetracycline, but not a shorter course, is effective for post-exposure prophylaxis.[120] Ciprofloxacin (or other fluoroquinolone) also is recommended.[92]

Botulinum Toxins

Clinical Features. Botulinum toxins are the most toxic substance known, with an inhalational LD50 of 3 ng/kg, approximately 100,000 times as toxic as sarin.[121] In addition, it is easy to manufacture and is well absorbed via aerosol.[122] A gram of botulinum toxin potentially could kill 1 million people. The quantity of botulinum produced by Iraq would have been sufficient to kill three times the total living human population.[123]

Naturally occurring food-borne outbreaks of botulism remain public health emergencies. While each outbreak averages 2.5 patients, approximately half have only a single victim.[123] The three largest outbreaks involved a total of 121 patients, illustrating the potential for even accidental poisonings to generate mass casualties, with half presenting with clinical symptoms to an ED.[124] Due to the implications of on-going exposure, the delayed and often insidious onset, and possible geographic dissemination, a nation-wide surveillance system is in place through the CDC.[125]

Most cases present within 36-72 hours (range 6 hours to 8 days) with an afebrile symmetric descending flaccid paralysis with a clear sensorium.[126,127] Depending on dose and route, the presentation can range from a subtle motor weakness to acute profound flaccid paralysis with respiratory arrest. The initial GI symptoms associated with food-borne outbreaks are thought to be due to other microbial by-products and would not be seen if purified toxin was released.[123,125]

Presenting complaints include weakness, blurred vision, diplopia, dry mouth, and dysarthria.[124] Facial muscle weakness and diminished ocular motility mimicking cranial neuropathies may result in a diagnostic delay. Typically, the initial sign of progression is a loss of head control. While the sensorium remains clear, and sensory features are uncommon, acral paresthesias due to hyperventilation are well described. Patients may appear obtunded due to the hypotonia.[123] Deep tendon reflexes may be

preserved initially, but diminish with progression, in sharp contrast to Guillain-Barré syndrome and the descending Miller-Fisher variant.[129] Constipation and urinary retention are common.[130] Ptosis and upper extremity weakness may indicate progression to the point that respiratory compromise may require mechanical ventilation.[131] Respiratory failure may be prolonged, typically requiring 2-8 weeks of ventilatory support.[128] Without mechanical ventilation, fatality rates are approximately 60%; with contemporary ICU care, the rate is now 5-10%.[126]

Prompt clinical diagnosis is critical. Delays and misdiagnosis are common and are associated with worse outcomes.[132,133] Other clinical entities with similar presentations that would suggest the need to consider botulism include myasthenic crisis, cholinergic crisis, Guillain-Barré syndrome, basilar artery insufficiency, tick paralysis, Eaton-Lambert syndrome, and various drug and toxin intoxications.[124,134,135] Prominent symmetric bulbar motor and anti-muscarinic features strongly support botulism.

Routine laboratory and radiographic studies are usually normal or non-diagnostic. However, serum chemistries may reveal other diagnoses, such as abnormalities of calcium or potassium, an elevated CPK suggesting a myopathic process, an elevated CSF protein suggesting Guillain-Barré syndrome, evidence of stroke or mass on computed tomography of the brain or CSF evidence of CNS infection, especially tuberculous or fungal meningitis.[128,136]

Urgent consultation with a neurologist in equivocal cases may facilitate diagnosis, as electomyogram (EMG) findings are highly suggestive.[137] Early clinical botulism may respond to anticholinesterase therapy similar to myasthenia gravis.[128,136] Serum samples should be collected (4-6 vacutainer tubes; red or tiger top) prior to administration of antitoxin or cholinesterase inhibitors, as it interferes with the gold-standard mouse bioassay.[123] The mouse bioassay is very sensitive and specific, but is time consuming and is not widely available. New diagnostic modalities remain limited.[138,139] The more sensitive stool cultures and PCR, while helpful in food-borne outbreaks, would not be helpful if preformed toxin was released intentionally.[140]

Treatment. If significant oral exposure is suspected, activated charcoal may be effective at reducing absorption.[141] Any exposed or symptomatic patients should be treated with antitoxin, admitted and followed closely for respiratory failure.[9,142,143] In cases of mass casualty exposure, the decision to withhold administration of antitoxin until development of symptoms may be necessary. Patients who present late in the course with stable or improving symptoms do not require antitoxin.[123]

Patients who are not mechanically ventilated should be cared for in a reverse Trendelenburg position with sufficient head and neck support to prevent airway occlusion. Patients admitted will require frequent neurologic assessments with careful attention to ability to handle secretions and otherwise protect their airway. Pulmonary function testing may show a decrease in vital capacity and inspiratory force prior to onset of hypercarbia.[144] Clindamycin and aminoglycoside antibiotics should not be administered because they may precipitously worsen neuromuscular function.[145-149] Succinylcholine should be used with caution.[150] Aspiration or loss of a patent airway usually precedes hypoventilation. The need for mechanical ventilation ranges from 20% to 60% of cases.[123] Once respiratory compromise occurs, treatment is mechanical ventilation, which usually is sufficiently prolonged to mandate tracheostomy.[131] Efforts to stockpile ventilators for emergency use are ongoing.[151] Recovery is prolonged with frequent complications associated with protracted immobilization and tracheal intubation.

There is a single commercially available antitoxin, a trivalent (containing anti-A, anti-B, and anti-E activity) equine preparation made only by Connaught Laboratories. Small-scale production of other products is limited to Japan and two European suppliers.[125] Given early in the course, it arrests progression of neurologic disease, shortens duration of mechanical ventilation and reduces mortality.[142] In one series, administration within 12 hours of presentation reduced intubation rates from 85% to 57% and duration of mechanical ventilation from a median of 54 days to 11 days.[131] Patients with significant wheal and flare will require intensive desensitization over several hours. While it is usually well tolerated, up to 9% of recipients will manifest typical serum sickness or urticaria and 2% will have life-threatening reactions.[152] A single vial will neutralize several lethal doses and is sufficient for naturally occurring botulism.[153] Additional doses theoretically may be needed following exposure to large amounts of purified toxin.

An investigational equine F(ab′)2 product with activity against toxin types A, B, C, D, E, and F has been developed and tested by the U.S. Army. It is available for clinical use under a compassionate use protocol.[154] Adjunctive therapy with guanidine or amino-pyridines is not effective.[155]

The trivalent equine antitoxin is stockpiled by the CDC in airports in New York, Chicago, Atlanta, Miami, Los Angeles, San Francisco, Seattle, and Honolulu. In addition, the state health departments of California and Alaska maintain their own stores. Additional stocks are held by the U.S. Army, and can be accessed by CDC officials. Canada maintains its own supply, but other members of the Pan American Health Organization are served by the CDC. This system allows most patients to be treated with antitoxin within 12 hours of contact with public health authorities.[125]

Any suspected case of botulism is a public health emergency. Local health departments work closely with the CDC's Food-borne and Diarrheal Disease Branch on a 24-hour-a-day basis. Emergency consultation, including diagnostic and treatment recommendations and provisions for antitoxin is available by calling (404) 639-2888.[125]

A formalin inactivated toxoid containing toxin types A, B, C, D, and E has been in use since the 1950s under an Investigational New Drug protocol to protect at-risk laboratory workers. It is safe and well tolerated, although the current product is rather painful on injection.

Although botulinum toxin has little potential for secondary aerosolization, aerosol release may require surface decontamination to avoid ingestion of persistent toxin.[121]

Use of Tetracyclines and Fluoroquinolones in Pregnant, Nursing, or Pediatric Patients

Although tetracyclines and fluoroquinolones usually are not used in children, nursing mothers, or pregnant women, their use for life-threatening infections is justified and recommended by the CDC, the Food and Drug Administration, the American Academy of Pediatrics, and the American College of Obstetricians and Gynecologists.[156-160] A growing body of literature on the safety of fluoroquinolones, particularly ciprofloxacin, suggests that risks are minimal and that clinicians should not hesitate to use them for serious infections.[161-169] Adverse effects of tetracyclines in pregnant women and in children are well described, but are acceptable in the face of life-threatening disease. In addition, doxycycline appears to be much safer than tetracycline, with no reports of untoward effects in children or in pregnancy.[170-173] Initiate therapy in children with ciprofloxacin (10-15 mg/kg/dose po q 12 hours not to exceed 1 g per day) or doxycycline (2.2 mg/kg/dose po BID not to exceed 100 mg po BID). If penicillin susceptibility is confirmed in a patient with anthrax, initiate or change to oral amoxicillin 80 mg/kg/day TID (maximum 500 mg/dose), or to trimethoprim sulfate if susceptible plague is isolated.[174]

Summary

Detection of a biological weapons attack hinges on a clinical suspicion, followed by laboratory investigations. Circumstances that should prompt immediate contact with surrounding EDs and urgent consultation with public health and law enforcement authorities include:

1) Any unusual temporal or spatial clustering of infectious diseases, especially if serious pulmonary symptoms or hemorrhagic diathesis are prominent or if stereotypical features are present;

2) Multiple, previously healthy patients with presentations of sepsis or fulminant pneumonia in otherwise healthy patients;

3) Clinical diagnosis or suspicion of smallpox;

4) Acute flaccid paralysis with prominent bulbar symptoms, suggesting botulism; and

5) Isolation of pathognomonic organisms; especially variola virus, agents of viral hemorrhagic fever, engineered or highly drug resistant *Bacillus anthracis, Yersinia pestis,* or isolation of genetically identical organisms from multiple regions.

There is little, if any, risk of contamination to health care workers following simple decontamination (removal of contaminated clothing and a soap and water shower). However, pneumonic plague, smallpox, and the viral hemorrhagic fevers present a substantial risk for secondary spread and explosive epidemics. Respiratory protection is required to care for these patients. Isolation or quarantine of cases and contacts is essential.

Viral cultures should be sent *only* to USAMRIID, CDC, or comparable facilities in other countries, via the local public health system.

Additional rapid and confirmatory diagnostic tests are available through the public health laboratory response network (NLRN).

Hospitals and EMS agencies should not participate in testing of environmental samples or materials suspected of harboring infectious agents. Any such concerns should be directed immediately to law enforcement agencies, which have the responsibility and expertise to address these issues.

References

1. Barquet N, Domingo P. Smallpox: The triumph over the most terrible of the ministers of death. *Ann Intern Med* 1997;127:635-642.
2. Breman JG, Henderson DA. Poxvirus dilemmas—Monkeypox, smallpox, and biologic terrorism. *N Engl J Med* 1998;339:556-559.
3. Henderson DA. The siren song of eradication. *J R Coll Physicians Lond* 1998;32:580-584.
4. Atlas RM. The threat of bioterrorism returns the fear of smallpox. *Curr Opin Microbiol* 1998;1:719-721.
5. Alibek K. *Biohazard: The Chilling True Story of the Largest Covert Biological Weapons Program in the World—Told from the Inside by the Man Who Ran It.* New York: Dell Publishing;1999.
6. Ellner PD. Smallpox: Gone but not forgotten. *Infection* 1998;26:263-269.
7. Associated Press. U.S. Accuses Six Nations of Developing Germ Weapons. *The New York Times*: November 19, 2001.
8. Henderson DA. Smallpox: Clinical and epidemiologic features. *Emerg Infect Dis* 1999;5:537-539.
9. Franz DR, Jahrling PB, McClain DJ, et al. Clinical recognition and management of patients exposed to biological warfare agents. *Clin Lab Med* 2001; 21:435-473.
10. McClain D. Smallpox. In: Sidell F, Takafuji E, Franz D, eds. *Medical Aspects of Chemical and Biological Warfare.* Washington, DC: Borden Institute, Walter Reed Army Medical Center;1997:539-558.
11. Henderson DA, Inglesby TV, Bartlett JG, et al. Smallpox as a biological weapon: Medical and public health management. Working Group on Civilian Biodefense. *JAMA* 1999;281:2127-2137.
12. Fenner F. Poxviruses. In: Fields B, Knipe D, Howely P, eds. *Fields Virology.* 3rd ed. Philadelphia: Lippincott-Raven;1996:2673-2702.
13. Jezek Z, Szczeniowski M, Paluku KM, et al. Human monkeypox: Clinical features of 282 patients. *J Infect Dis* 1987;156:293-298.
14. McGovern TW, Christopher GW, Eitzen EM. Cutaneous manifestations of biological warfare and related threat agents. *Arch Dermatol* 1999;135: 311-322.
15. Jahrling PB ZG, Huggins JW. Countermeasures to the reemergence of smallpox virus as an agent of bioterrorism. *Emerg Infect* 2000;4:187-200.
16. Bray M, Martinez M, Smee DF, et al. Cidofovir protects mice against lethal aerosol or intranasal cowpox virus challenge. *J Infect Dis* 2000;181:10-19.
17. Keating MR. Antiviral agents for non-human immunodeficiency virus infections. *Mayo Clin Proc* 1999;74:1266-1283.
18. De Clercq E. Vaccinia virus inhibitors as a paradigm for the chemo-therapy of poxvirus infections. *Clin Microbiol Rev* 2001;14:382-397.
19. Cohen J, Marshall E. Bioterrorism: Vaccines for biodefense. A system in distress. *Science* 2001;294:498-501.
20. Centers for Disease Control and Prevention. Vaccinia (Smallpox) Vaccine: Recommendations of the Advisory Commitee on Immunization Practices (ACIP), 2001. Atlanta, GA: CDC; 2001:RR-10.
21. Lane JM, Ruben FL, Neff JM, et al. Complications of smallpox vaccination, 1968: results of ten statewide surveys. *J Infect Dis* 1970;122:303-309.
22. Ruben FL, Lane JM. Ocular vaccinia. An epidemiologic analysis of 348 cases. *Arch Ophthalmol* 1970;84:45-48.
23. World Health Organization. Outbreak News. *Wkly Epidemiol Rec* 2002;77:1-9.
24. Borio L, Inglesby T, Peters CJ, et al. Hemorrhagic fever viruses as biological weapons: medical and public health management. *JAMA* 2002;287: 2391-2405.
25. Burgess TH, Steele KE, Schoneboom BA, Grieder FB. Clinicopathologic features of viral agents of potential use by bioterrorists. *Clin Lab Med* 2001; 21:475-493.
26. Peters C. Are hemorrhagic fever viruses practical agents for biological terrorism? *Emerg Infect Dis* 2000;4:201-209.

27. Khan AS, Tshioko FK, Heymann DL, et al. The reemergence of Ebola hemorrhagic fever, Democratic Republic of the Congo, 1995. *J Infect Dis* 1999; 179(Suppl 1):S76-86.
28. Amblard J, Obiang P, Edzang S, et al. Identification of the Ebola virus in Gabon in 1994. *Lancet* 1997;349:181-182.
29. Le Guenno B, Formenty P, Boesch C. Ebola virus outbreaks in the Ivory Coast and Liberia, 1994-1995. *Curr Top Microbiol Immunol* 1999;235:77-84.
30. Georges AJ, Leroy EM, Renaut AA, et al. Ebola hemorrhagic fever outbreaks in Gabon, 1994-1997: Epidemiologic and health control issues. *J Infect Dis* 1999;179(Suppl 1):S65-75.
31. Fatal illnesses associated with a new world arenavirus—California, 1999-2000. *MMWR Morb Mortal Wkly Rep* 2000;49(31):709-711.
32. Doyle TJ, Bryan RT, Peters CJ. Viral hemorrhagic fevers and hantavirus infections in the Americas. I*nfect Dis Clin North Am* 1998;12:95-110.
33. Isaacson M. Viral hemorrhagic fever hazards for travelers in Africa. *Clin Infect Dis* 2001;33:1707-1712.
34. McCormick JB, Webb PA, Krebs JW, et al. A prospective study of the epidemiology and ecology of Lassa fever. *J Infect Dis* 1987;155:437-444.
35. Weber D, Rutala W. Risks and prevention of nosocomial transmission of rare zoonotic diseases. *Clin Infect Dis* 2001;32:446-456.
36. Zaki SR, Goldsmith CS. Pathologic features of filovirus infections in humans. *Curr Top Microbiol Immunol* 1999;235:97-116.
37. Chepurnov AA, Tuzova MN, Ternovoy VA, et al. Suppressive effect of Ebola virus on T-cell proliferation in vitro is provided by a 125-kDa GP viral protein. *Immunol Lett* 1999;68:257-261.
38. Yang ZY, Duckers HJ, Sullivan NJ, et al. Identification of the Ebola virus glycoprotein as the main viral determinant of vascular cell cytotoxicity and injury. *Nat Med* 2000;6:886-889.
39. Fisher-Hoch SP, Platt GS, Lloyd G, et al. Haematological and biochemical monitoring of Ebola infection in rhesus monkeys: Implications for patient management. *Lancet* 1983;2:1055-1058.
40. Ishak KG, Walker DH, Coetzer JA, et al. Viral hemorrhagic fevers with hepatic involvement: Pathologic aspects with clinical correlations. *Prog Liver Dis* 1982;7:495-515.
41. Formenty P, Hatz C, Le Guenno B, et al. Human infection due to Ebola virus, subtype Cote d'Ivoire: Clinical and biologic presentation. *J Infect Dis* 1999;179(Suppl 1):S48-53.
42. Bwaka MA, Bonnet MJ, Calain P, et al. Ebola hemorrhagic fever in Kikwit, Democratic Republic of the Congo: Clinical observations in 103 patients. *J Infect Dis* 1999;179(Suppl 1):S1-7.
43. Rowe AK, Bertolli J, Khan AS, et al. Clinical, virologic, and immunologic follow-up of convalescent Ebola hemorrhagic fever patients and their household contacts, Kikwit, Democratic Republic of the Congo. Commission de Lutte contre les Epidémies ; Kikwit. *J Infect Dis* 1999;179(Suppl 1):S28-35.
44. Gear JS, Cassel GA, Gear AJ, et al. Outbreake of Marburg virus disease in Johannesburg. *BMJ* 1975;4:489-493.
45. Smith DH, Johnson BK, Isaacson M, et al. Marburg-virus disease in Kenya. *Lancet* 1982;1:816-820.
46. Walker DH, McCormick JB, Johnson KM, et al. Pathologic and virologic study of fatal Lassa fever in man. *Am J Pathol* 1982; 107:349-356.
47. Dowell SF, Mukunu R, Ksiazek TG, et al. Transmission of Ebola hemorrhagic fever: A study of risk factors in family members, Kikwit, Democratic Republic of the Congo, 1995. Commission de Lutte contre les Epidémies; Kikwit. *J Infect Dis* 1999;179(Suppl 1):S87-91.
48. Kerstiens B, Matthys F. Interventions to control virus transmission during an outbreak of Ebola hemorrhagic fever: Experience from Kikwit, Democratic Republic of the Congo, 1995. *J Infect Dis* 1999;179(Suppl 1):S263-267.
49. Rollin PE, Williams RJ, Bressler DS, et al. Ebola (subtype Reston) virus among quarantined nonhuman primates recently imported from the Philippines to the United States. *J Infect Dis* 1999;179: S108-114.
50. Jaax N, Jahrling P, Geisbert T, et al. Transmission of Ebola virus (Zaire strain) to uninfected control monkeys in a biocontainment laboratory. *Lancet* 1995;346:1669-1671.
51. Enria D, Bowen MD, Mills JN, et al. Arenavirus Infections. In: Guerrant RL, Walker DH, Weller PF, eds. *Tropical Infectious Diseases: Principles, Pathogens, and Practice.* New York, NY: W.B. Saunders Co; 1999:1191-1212.
52. Update: Management of patients with suspected viral hemorrhagic fever—United States. *MMWR Morb Mortal Wkly Rep* 1995;44:475-479.
53. Speed BR, Gerrard MP, Kennett ML, et al. Viral haemorrhagic fevers: Current status, future threats. *Med J Aust* 1996;164:79-83.
54. Harrison LH, Halsey NA, McKee KT Jr, et al. Clinical case definitions for Argentine hemorrhagic fever. *Clin Infect Dis* 1999;28:1091-1094.
55. de Manzione N, Salas RA, Paredes H, et al. Venezuelan hemorrhagic fever: Clinical and epidemiological studies of 165 cases. *Clin Infect Dis* 1998; 26:308-313.
56. Schwarz TF, Nsanze H, Ameen AM. Clinical features of Crimean-Congo haemorrhagic fever in the United Arab Emirates. *Infection* 1997;25:364-367.
57. Vainrub B, Salas R. Latin American hemorrhagic fever. *Infect Dis Clin North Am* 1994;8:47-59.
58. Sanchez A, Peters C, Zaki S, et al. Filovirus Infections. In: Guerrant RL, Walker DH, Weller PF, eds. *Tropical Infectious Diseases: Principles, Pathogens, and Practice* New York, NY: W.B. Saunders Co; 1999:1240-1252.
59. Khan AS, Sanchez A, Pflieger AK. Filoviral haemorrhagic fevers. *Br Med Bull* 1998;54:675-692.
60. Peters CJ, Buchmeier MJ, Rollin PE, et al. Arenaviruses. In: Fields B, Knipe D, Howely P, eds. *Fields Virology*. 3rd ed. Philadelphia: Lippincott-Raven; 1996:1521-1551.
61. Frame JD. Clinical features of Lassa fever in Liberia. *Rev Infect Dis* 1989;11 Suppl 4:S783-789.
62. Monson MH, Frame JD, Jahrling PB, et al. Endemic Lassa fever in Liberia. I: Clinical and epidemiological aspects at Curran Lutheran Hospital, Zorzor, Liberia. *Trans R Soc Trop Med Hyg* 1984;78:549-553.
63. Knobloch J, McCormick JB, Webb PA, et al. Clinical observations in 42 patients with Lassa fever. *Tropenmed Parasitol* 1980;31:389-398.
64. McCormick JB, King IJ, Webb PA, et al. A case-control study of the clinical diagnosis and course of Lassa fever. *J Infect Dis* 1987;155:445-455.
65. Price ME, Fisher-Hoch SP, Craven RB, et al. A prospective study of maternal and fetal outcome in acute Lassa fever infection during pregnancy. *BMJ* 1988;297:584-587.
66. Fisher-Hoch S, McCormick JB, Sasso D, et al. Hematologic dysfunction in Lassa fever. *J Med Virol* 1988;26:127-135.
67. Fisher-Hoch SP, McCormick JB. Pathophysiology and treatment of Lassa fever. *Curr Top Microbiol Immunol* 1987;134:231-239.
68. McCormick JB, King IJ, Webb PA, et al. Lassa fever. Effective therapy with ribavirin. *N Engl J Med* 1986;314:20-26.
69. Colebunders R, Borchert M. Ebola haemorrhagic fever—A review. *J Infect* 2000;40:16-20.
70. ter Meulen J. Response to haemorrhagic fevers in Europe. *Lancet* 2000;356 (Suppl):S64.
71. Chen JP, Cosgriff TM. Hemorrhagic fever virus-induced changes in hemostasis and vascular biology. *Blood Coagul Fibrinolysis* 2000;11:461-483.
72. Heller MV, Marta RF, Sturk A, et al. Early markers of blood coagulation and fibrinolysis activation in Argentine hemorrhagic fever. *Thromb Haemost* 1995;73:368-373.
73. Molinas FC, de Bracco MM, Maiztegui JI. Hemostasis and the complement system in Argentine hemorrhagic fever. *Rev Infect Dis* 1989;11(Suppl 4): S762-770.
74. Loutfy MR, Assmar M, Hay Burgess DC, et al. Effects of viral hemorrhagic fever inactivation methods on the performance of rapid diagnostic tests for Plasmodium falciparum. *J Infect Dis* 1998;178:1852-1855.
75. Mitchell SW, McCormick JB. Physicochemical inactivation of Lassa, Ebola, and Marburg viruses and effect on clinical laboratory analyses. *J Clin Microbiol* 1984;20:486-489.
76. Jahrling PB, Geisbert TW, Geisbert JB, et al. Evaluation of immune globulin and recombinant interferon-alpha2b for treatment of experimental Ebola virus infections. *J Infect Dis* 1999;179:S224-234.
77. Kudoyarova-Zubavichene NM, Sergeyev NN, Chepurnov AA, et al. Preparation and use of hyperimmune serum for prophylaxis and therapy of Ebola virus infections. *J Infect Dis* 1999;179:S218-223.
78. Mupapa K, Massamba M, Kibadi K, et al. Treatment of Ebola hemorrhagic

fever with blood transfusions from convalescent patients. International Scientific and Technical Committee. *J Infect Dis* 1999;179:S18-23.
79. Huggins JW. Prospects for treatment of viral hemorrhagic fevers with ribavirin, a broad-spectrum antiviral drug. *Rev Infect Dis* 1989;11:S750-761.
80. Bray M, Driscoll J, Huggins JW. Treatment of lethal Ebola virus infection in mice with a single dose of an S-adenosyl-L-homocysteine hydrolase inhibitor. *Antiviral Research* 2000;45:135-147.
81. Huggins J, Zhang ZX, Bray M. Antiviral drug therapy of filovirus infections: S-adenosylhomocysteine hydrolase inhibitors inhibit Ebola virus in vitro and in a lethal mouse model. *J Infect Dis* 1999;179(Suppl 1):S240-247.
82. Enria DA, Briggiler AM, Fernandez NJ. Importance of dose of neutralising antibodies in treatment of Argentine haemorrhagic fever with immune plasma. *Lancet* 1984;2:255-256.
83. Enria DA, Maiztegui JI. Antiviral treatment of Argentine hemorrhagic fever. *Antiviral Research* 1994;23:23-31.
84. Maiztegui JI, Fernandez NJ, de Damilano AJ. Efficacy of immune plasma in treatment of Argentine haemorrhagic fever and association between treatment and a late neurological syndrome. *Lancet* 1979;2:1216-1217.
85. Snell NJ. Ribavirin—Current status of a broad spectrum antiviral agent. *Expert Opin Pharmacother* 2001;2:1317-1324.
86. Kilgore PE, Ksiazek TG, Rollin PE, et al. Treatment of Bolivian hemorrhagic fever with intravenous ribavirin. *Clin Infect Dis* 1997;24:718-722.
87. Fisher-Hoch SP, Khan JA, Rehman S. Crimean Congo-haemorrhagic fever treated with oral ribavirin. *Lancet* 1995;346:472-475.
88. Barry M, Russi M, Armstrong L, et al. Brief report: Treatment of a laboratory-acquired Sabia virus infection. *N Engl J Med* 1995;333:294-296.
89. Moss JT, Wilson JP. Treatment of viral hemorrhagic fevers with ribavirin. *Ann Pharmacother* 1992;26:1156-1157.
90. McKee KT Jr, Huggins JW, Trahan CJ, et al. Ribavirin prophylaxis and therapy for experimental argentine hemorrhagic fever. *Antimicrob Agents Chemother* 1988;32:1304-1309.
91. Feldman KA, Enscore RE, Lathrop SL, et al. An outbreak of primary pneumonic tularemia on Martha's Vineyard. *N Engl J Med* 2001;345: 1601-1606.
92. Dennis DT, Inglesby TV, Henderson DA, et al. Tularemia as a biological weapon: Medical and public health management. *JAMA* 2001;285: 2763-2773.
93. Martin GJ, Marty AM. Clinicopathologic aspects of bacterial agents. *Clin Lab Med* 2001;21:513-548, ix.
94. Evans ME, Fridlander A. Tularemia. In: Sidell F, Takafuki E, Franz D, eds. *Medical Aspects of Chemical and Biological Warfare.* Washington, DC: Borden Institute, Walter Reed Army Medical Center;1997:503-512.
95. Evans ME, Gregory DW, Schaffner W, et al. Tularemia: A 30-year experience with 88 cases. *Medicine* 1985;64:251-269.
96. Sanders CV, Hahn R. Analysis of 106 cases of tularemia. J *La State Med Soc* Sep 1968;120:391-393.
97. Harrell RE, Whitaker GR. Tularemia: Emergency department presentation of an infrequently recognized disease. *Am J Emerg Med* 1985;3:415-418.
98. Anonymous. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 14-2000. A 60-year-old farm worker with bilateral pneumonia. *N Engl J Med* 2000;342:1430-1438.
99. Gill V, Cunha BA. Tularemia pneumonia. *Sem Respir Infect* 1997;12:61-67.
100. Fredricks DN, Remington JS. Tularemia presenting as community-acquired pneumonia. Implications in the era of managed care. *Arch Intern Med* 1996; 156:2137-2140.
101. Luotonen J, Syrjala H, Jokinen K, et al. Tularemia in otolaryngologic practice. An analysis of 127 cases. *Arch Otolaryngol Head Neck Surg* 1986; 112:77-80.
102. Jacobs RF, Condrey YM, Yamauchi T. Tularemia in adults and children: A changing presentation. *Pediatrics* 1985;76:818-822.
103. Steinemann TL, Sheikholeslami MR, Brown HH, et al. Oculoglandular tularemia. *Arch Ophthalmol* 1999;117:132-133.
104. Cerny Z. Skin manifestations of tularemia. *Int J Dermatol* 1994;33:468-470.
105. Evans ME. Francisella tularensis. *Infect Cont* 1985;6:381-383.
106. Doern GV, Davaro R, George M, et al. Lack of requirement for prolonged incubation of Septi-Chek blood culture bottles in patients with bacteremia due to fastidious bacteria. *Diagn Microbiol Infect Dis* Mar 1996;24:141-143.
107. Brion JP, Recule C, Croize J, et al. Isolation of *Francisella tularensis* from lymph node aspirate inoculated into a non-radiometric blood culture system. *Eur J Clin Microbiol Infect Dis* 1996;15:180-181.
108. Syrjala H, Koskela P, Ripatti T, et al. Agglutination and ELISA methods in the diagnosis of tularemia in different clinical forms and severities of the disease. *J Infect Dis* 1986;153:142-145.
109. Karhukorpi EK, Karhukorpi J. Rapid laboratory diagnosis of ulceroglandular tularemia with polymerase chain reaction. *Scand J Infect Dis* 2001;33: 383-385.
110. Memish Z, Oni G, Mah M. The correlation of agglutination titer with positive blood cultures in brucellosis: A comparison of two study periods. *J Chemother* 2001;13 Suppl 1:60-1.
111. Johansson A, Berglund L, Eriksson U, et al. Comparative analysis of PCR versus culture for diagnosis of ulceroglandular tularemia. *J Clin Microbiol* 2000;38:22-26.
112. Penn RL, Kinasewitz GT. Factors associated with a poor outcome in tularemia. *Arch Int Med* 1987;147:265-268.
113. Cross JT Jr., Schutze GE, Jacobs RF. Treatment of tularemia with gentamicin in pediatric patients. *Pediatr Infect Dis J* 1995;14:151-152.
114. Enderlin G, Morales L, Jacobs RF, et al. Streptomycin and alternative agents for the treatment of tularemia: Review of the literature. *Clin Infect Dis* 1994; 19:42-47.
115. Cross JT, Jacobs RF. Tularemia: Treatment failures with outpatient use of ceftriaxone. *Clin Infect Dis* 1993;17:976-980.
116. Perez-Castrillon JL, Bachiller-Luque P, Martin-Luquero M, et al. Tularemia epidemic in northwestern Spain: Clinical description and therapeutic response. *Clin Infect Dis* 2001;33:573-576.
117. Russell P, Eley SM, Fulop MJ, et al. The efficacy of ciprofloxacin and doxycycline against experimental tularaemia. *J Antimicrob Chemother* 1998; 41:461-465.
118. Rodgers BL, Duffield RP, Taylor T, et al. Tularemic meningitis. *Pediatr Infect Dis J* May 1998;17:439-441.
119. Johansson A, Berglund L, Sjostedt A, et al. Ciprofloxacin for treatment of tularemia. *Clin Infect Dis* 2001;33:267-268.
120. Sawyer WD, Dangerfield HG, Hogge AL, et al. Antibiotic prophylaxis and therapy of airborne tularemia. *Bacteriol Rev* 1966;30:542-550.
121. Madsen JM. Toxins as weapons of mass destruction. A comparison and contrast with biological-warfare and chemical-warfare agents. *Clin Lab Med* 2001;21:593-605.
122. Middlebrook JL, Franz D. Botulinum Toxins. In: Sidell F, Takafuki E, Franz D, eds. *Medical Aspects of Chemical and Biological Warfare*. Washington, DC: Borden Institute, Walter Reed Army Medical Center; 1997:643-654.
123. Arnon SS, Schechter R, Inglesby TV, et al. Botulinum toxin as a biological weapon: Medical and public health management. *JAMA* 2001;285:1059-1070.
124. Ruthman JC, Hendricksen DK, Bonefeld R. Emergency department presentation of type A botulism. *Am J Emerg Med* 1985;3:203-205.
125. Shapiro RL, Hatheway C, Becher J, et al. Botulism surveillance and emergency response. A public health strategy for a global challenge. *JAMA* 1997;278:433-435.
126. Hughes JM, Blumenthal JR, Merson MH, et al. Clinical features of types A and B food-borne botulism. *Ann Intern Med* 1981;95:442-445.
127. Terranova W, Breman JG, Locey RP, et al. Botulism type B: Epidemiologic aspects of an extensive outbreak. *Am J Epidemiol* 1978;108:150-156.
128. Shapiro RL, Hatheway C, Swerdlow DL. Botulism in the United States: A clinical and epidemiologic review. *Ann Intern Med* 1998;129:221-228.
129. Maselli RA, Ellis W, Mandler RN, et al. Cluster of wound botulism in California: Clinical, electrophysiologic, and pathologic study. *Muscle Nerve* 1997;20:1284-1295.
130. Sautter T, Herzog A, Hauri D, et al. Transient paralysis of the bladder due to wound botulism. *Euro Urol* 2001;39:610-612.
131. Sandrock CE, Murin S. Clinical predictors of respiratory failure and long-term outcome in black tar heroin-associated wound botulism. *Chest* 2001; 120:562-566.

132. Mitchell PA, Pons PT. Wound botulism associated with black tar heroin and lower extremity cellulitis. *J Emerg Med* 2001;20:371-375.
133. Burningham MD, Walter FG, Mechem C, et al. Wound botulism. *Ann Emerg Med* 1994;24:1184-1187.
134. Greenaway C, Orr P. A foodborne outbreak causing a cholinergic syndrome. *J Emerg Med* 1996;14:339-344.
135. Susuki K, Takahashi H, Yuki N, et al. Guillain-Barre syndrome mimicking botulism. *J Neurol* 2001;248:720-721.
136. LoVecchio F, Jacobson S. Approach to generalized weakness and peripheral neuromuscular disease. *Emerg Med Clin North Am* 1997;15:605-623.
137. Padua L, Aprile I, Monaco ML, et al. Neurophysiological assessment in the diagnosis of botulism: Usefulness of single-fiber EMG. *Muscle Nerve* 1999; 22:1388-1392.
138. O'Brien T, Johnson LH 3rd, Aldrich JL, et al. The development of immunoassays to four biological threat agents in a bidiffractive grating biosensor. *Biosensors Bioelectron* 2000;14:815-828.
139. Ferreira JL, Eliasberg SJ, Harrison MA, et al. Detection of preformed type A botulinal toxin in hash brown potatoes by using the mouse bioasssay and a modified ELISA test. *J AOAC Internat* 2001;84:1460-1464.
140. Lindstrom M, Keto R, Markkula A, et al. Multiplex PCR assay for detection and identification of *Clostridium botulinum* types A, B, E, and F in food and fecal material. *Appl Environ Microbiol* 2001;67:5694-5699.
141. Gomez HF, Johnson R, Guven H, et al. Adsorption of botulinum toxin to activated charcoal with a mouse bioassay. *Ann Emerg Med* 1995;25:818-822.
142. Tacket CO, Shandera WX, Mann JM, et al. Equine antitoxin use and other factors that predict outcome in type A foodborne botulism. *Am J Med* 1984; 76:794-798.
143. Franz DR, Jahrling PB, Friedlander AM, et al. Clinical recognition and management of patients exposed to biological warfare agents. JAMA 1997;278: 399-411.
144. Anderson MW, Sharma K, Feeney CM. Wound botulism associated with black tar heroin. *Acad Emerg Med* 1997;4:805-809.
145. Santos JI, Swensen P, Glasgow LA. Potentiation of *Clostridium botulinum* toxin aminoglycoside antibiotics: Clinical and laboratory observations. *Pediatrics* 1981;68:50-54.
146. L'Hommedieu C, Stough R, Brown L, et al. Potentiation of neuromuscular weakness in infant botulism by aminoglycosides. *J Pediatr* 1979;95: 1065-1070.
147. Schwartz RH, Eng G. Infant botulism: Exacerbation by aminoglycosides. *Am J Dis Child* 1982;136:952.
148. Wang YC, Burr DH, Korthals GJ, et al. Acute toxicity of aminoglycoside antibiotics as an aid in detecting botulism. *Appl Environ Microbiol* 1984; 48:951-955.
149. Schulze J, Toepfer M, Schroff KC, et al. Clindamycin and nicotinic neuromuscular transmission. *Lancet* 1999;354:1792-1793.
150. Chakravarty EF, Kirsch CM, Jensen WA, et al. Cardiac arrest due to succinylcholine-induced hyperkalemia in a patient with wound botulism. *J Clin Anesth* 2000;12:80-82.
151. Khan AS, Morse S, Lillibridge S. Public-health preparedness for biological terrorism in the USA. *Lancet* 2000;356:1179-1182.
152. Black RE, Gunn RA. Hypersensitivity reactions associated with botulinal antitoxin. *Am J Med* 1980;69:567-570.
153. Hatheway CH, Snyder JD, Seals JE, et al. Antitoxin levels in botulism patients treated with trivalent equine botulism antitoxin to toxin types A, B, and E. *J Infect Dis* 1984;150:407-412.
154. Hibbs RG, Weber JT, Corwin A, et al. Experience with the use of an investigational F(ab′)2 heptavalent botulism immune globulin of equine origin during an outbreak of type E botulism in Egypt. *Clin Infect Dis* 1996;23:337-340.
155. Adler M, Keller JE, Baskin S, et al. Promising new approaches for treatment of botulinum intoxication. *J Appl Toxicol* 1999;19(Suppl 1):S3-4.
156. Committee on Drugs AAOP. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001;108:776-789.
157. Update: Interim recommendations for antimicrobial prophylaxis for children and breastfeeding mothers and treatment of children with anthrax. *MMWR Morb Mortal Wkly Rep* 2001;50:1014-1016.
158. Updated recommendations for antimicrobial prophylaxis among asymptomatic pregnant women after exposure to *Bacillus anthracis. MMWR Morb Mortal Wkly Rep* 2001;50:960.
159. Benavides S, Nahata MC. Anthrax: Safe treatment for children. *Ann Pharmacother* 2002;36:334-337.
160. ACOG Committee Opinion number 268, February 2002. Management of asymptomatic pregnant or lactating women exposed to anthrax. American College of Obstetrics and Gynecology. *Obstetric Gynecol* 2002;99:366-368.
161. Schaefer C, Amoura-Elefant E, Vial T, et al. Pregnancy outcome after prenatal quinolone exposure. Evaluation of a case registry of the European Network of Teratology Information Services (ENTIS). *Eur J Obstet Gynecol Reprod Biol* 1996;69:83-89.
162. Loebstein R, Addis A, Ho E, et al. Pregnancy outcome following gestational exposure to fluoroquinolones: A multicenter prospective controlled study. *Antimicrob Agents Chemother* 1998;42:1336-1339.
163. Richard DA, Nousia-Arvanitakis S, Sollich V, et al. Oral ciprofloxacin vs. intravenous ceftazidime plus tobramycin in pediatric cystic fibrosis patients: Comparison of antipseudomonas efficacy and assessment of safety with ultrasonography and magnetic resonance imaging. Cystic Fibrosis Study Group. *Pediatr Infect Dis J* 1997;16:572-578.
164. Redmond AO. Risk-benefit experience of ciprofloxacin use in pediatric patients in the United Kingdom. *Pediatr Infect Dis J* 1997;16:147-149; discussion 160-162.
165. Freifeld A, Pizzo P. Use of fluoroquinolones for empirical management of febrile neutropenia in pediatric cancer patients. *Pediatr Infect Dis J* 1997; 16:140-145; discussion 145-146, 160-162.
166. Jick S. Ciprofloxacin safety in a pediatric population. *Pediatr Infect Dis J* 1997;16:130-133; discussion 133-134, 160-162.
167. Hampel B, Hullmann R, Schmidt H. Ciprofloxacin in pediatrics: worldwide clinical experience based on compassionate use—Safety report. *Pediatr Infect Dis J* 1997;16:127-129; discussion 160-162.
168. Koul PA, Wani JI, Wahid A. Ciprofloxacin for multiresistant enteric fever in pregnancy. *Lancet* 1995;346:307-308.
169. Berkovitch M, Pastuszak A, Gazarian M, et al. Safety of the new quinolones in pregnancy. *Obstetr Gynecol* 1994;84:535-538.
170. Czeizel AE, Rockenbauer M. Teratogenic study of doxycycline. *Obstetr Gynecol* 1997;89:524-528.
171. Anonymous. Chemical-biological terrorism and its impact on children: A subject review. American Academy of Pediatrics. Committee on Environmental Health and Committee on Infectious Diseases. *Pediatrics* 2000; 105:662-670.
172. Briggs GG, Freeman RK, Yaffe SJ. *Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk.* 5th ed. Baltimore: Williams & Wilkins;1998.
173. Friedman JM, Polifka JE. *Teratogenic Effects of Drugs: A Resource for Clinicians (TERIS)*. 2nd ed. Baltimore: Johns Hopkins University Press; 2000.
174. American Academy of Pediatrics. *Red Book 2000: Report of the Committee on Infectious Diseases*. 25th ed. Chicago, IL: American Academy Of Pediatrics; 2000.

Physician CME Questions

To earn CME credit for this issue of Trauma Reports*, please refer to the enclosed Scantron form for directions on taking the test and submitting your answers.*

1. Which of the following is true regarding smallpox?
   A. The predominant method of transmission is by respiratory droplets.
   B. Smallpox is minimally contagious.
   C. Infectivity is not increased in patients with smallpox and a cough.
   D. Variola minor strains have the highest mortality rates.
   E. Variola minor lesions usually are larger than variola major.

2. Which of the following is/are true regarding the management of smallpox?
   A. Strict isolation is essential.
   B. Treatment largely is supportive.
   C. Anyone exposed to a patient with contagious smallpox should be vaccinated and quarantined for 17 days.
   D. Antiviral therapy historically has not been useful.
   E. All of the above

3. Which of the following is true regarding vaccination following exposure to a patient with contagious smallpox?
   A. An individual vaccinated 1 year ago requires a repeat dose of the vaccine.
   B. An exposed individual optimally should be vaccinated within 2-3 days of exposure.
   C. An individual vaccinated six years ago does not require a second dose of the vaccine.
   D. VIG is a highly effective post-exposure prophylactic agent.
   E. VIG is very effective against post-vaccination encephalitis.

4. Which of the following is a potentially serious complication associated with the smallpox vaccine?
   A. Urticarial eruptions
   B. Erythema multiforme
   C. Accidental inoculation of the eye
   D. Generalized vaccina in a non-immunocompromised host
   E. Mild systemic symptoms and regional lymphadenopathy

5. Which of the following is/are true regarding filoviruses?
   A. The filoviruses are associated with a high level of viremia.
   B. Thrombocytopenia and lymphopenia may occur.
   C. Hepatopathy without icterus may be present.
   D. Myocarditis is common.
   E. All of the above.

6. Which of the following is *not* typical for the presentation of a patient with a VHF infection?
   A. Severe tachycardia
   B. Myalgias
   C. Headache
   D. Orthostatic symptoms
   E. Hypovolemia

CME Objectives

Upon completing this program, the participants will be able to:

a.) Recognize or increase index of suspicion for diseases that may result from biological terrorism;

b.) Be educated about rapid stabilization, and the isolation of patients with exposure to or evidence of smallpox, viral hemorrhagic fevers, tularemia, and botulinum toxins;

c.) Understand various diagnostic and treatment modalities for diseases associated with biowarfare; and

d.) Understand both likely and rare complications that may occur.

7. Which of the following is true regarding AHF?
   A. It is an uncommon South American filovirus.
   B. Its onset typically is acute.
   C. Sore throat, nasal congestion, and cough typically are present.
   D. Patients often develop neurologic disease within a week of presentation.
   E. Treatment with immune plasma or ribavirin is ineffective.

8. Which of the following is true of management of a patient with VHF infection?
   A. Interferon decreases the duration of the illness.
   B. Antibody preparations reduce the infectivity of the patient.
   C. Ribavirin inhibits arenaviruses, RVF, and CCHF.
   D. Barrier nursing is not necessary.
   E. Invasive procedures and IM injections may be performed without caution.

9. Which of the following is/are associated with botulism?
   A. Weakness
   B. Blurred vision
   C. Dysarthria
   D. Facial muscle weakness
   E. All of the above

10. Which of the following is true regarding the diagnostic work-up of a patient with potential botulism?
   A. Routine laboratory studies are typically normal or non-diagnostic.
   B. CPK usually is elevated.
   C. CSF protein usually is high.
   D. CT scan of the brain may show diffuse edema.
   E. EMG findings typically are not helpful.

In Future Issues: **Rapid Sequence Intubation**

Summary of Major Agents

DISEASE	CLINICAL PRESENTATION	DIAGNOSTIC STUDIES	TREATMENT
Anthrax			
Inhalational	Nonspecific prodrome of fever, dyspnea, cough, retrosternal chest discomfort followed by respiratory failure and hemodynamic collapse. Mediastinal widening universal in late stage, pulmonary infiltrate seen in up to 25% and meningitis in 50%.	Blood culture and Gram stain, CSF Gram stain and culture, chest x-ray or CT, antigenemia by ELISA/PCR/CL	Ciprofloxacin (other fluoroquinolones likely effective, but largely untested; penicillin (amoxicillin acceptable); gentamycin or streptomycin. Add chloramphenicol if evidence of meningitis. Bodily fluids and secretions may generate spores if left in contact with air, and must be disinfected (e.g., soaked in bleach, incinerated, autoclaved). Aspiration of pustule may increase risk of bacteremia. Steroids effective for controlling edema, if required for airway impingement.
Cutaneous	Pruritic papule that progresses to pustule. Local edema and adenopathy common.	Gram stain and culture from under eschar	
Pneumonic plague	Fulminant pneumonia with hemoptysis, sepsis, and disseminated intravascular coagulation (DIC)	Sputum for Gram stain, culture, IFA	*Respiratory protection and droplet precautions (isolation room or cohort).* Avoid lactam antibiotics, if possible. Streptomycin or gentamycin with chloramphenicol for meningitis. Tetracyclines effective. Quinolones likely effective, but unproven. TMP/SMZ less effective.
Botulism	Bulbar neuropathy (diplopia, ptosis, dysarthria), mydriasis, xerostomia followed by descending paralysis with preserved cognition with respiratory failure in 12-72 hrs. Afebrile.	EMG helpful but not diagnostic; may see response to edrophonium, difficult to detect in serum.	Intubation for respiratory failure. If antitoxin is given, it will arrest progression, shorten requirement for mechanical ventilation, and reduce mortality.
Smallpox	Severe prostrating febrile illness with synchronous evolution of pustules, particularly on face and arms.	Pharyngeal swabs or scabs (BSL-4)	Cidofovir effective in mice. Vaccinia immune globulin 0.6 mL/kg IM within 72 hours of exposure in conjunction with Vaccinia vaccine. *Isolation essential to prevent dissemination.*
Pneumonic tularemia	Acute, nonspecific febrile illness with ulcerations, pharyngitis, and pneumonia	Blood, pharyngeal, or ulcer swabs for culture or PCR; serology	Gentamycin or streptomycin. Ciprofloxacin (other fluoroquinolones likely effective, but largely untested); doxycycline (or other tetracycline) less effective. Add chloramphenicol if evidence of meningitis.
Filovirus hemorrhagic fever	Severe disease, marked weight loss, prostration, late encephalopathy, and bleeding. Often see maculopapular rash. 25-90% case fatality.	Viral antigen in blood. Viral isolation	Supportive. *Isolation essential to prevent dissemination.*
Arenavirus hemorrhagic fever	Prostration, shock, bleeding, CNS disease (less common in Lassa fever). Thrombocytopenia, leukopenia, and proteinuria.	Viral antigen or IgM detection; viral isolation	Ribavirin. High titer plasma for AHF no longer readily available. Isolation advisable, at least droplet precautions.
Brucellosis	Protracted recurrent fever, depression, fatigue, myalgias, arthritis, endocarditis, meningitis, sacroiliitis, orchitis, and septic abortion. Cytopenias common.	Blood or bone marrow culture. PCR. Serology by ELISA, agglutination, or dipstick assay.	Prolonged treatment with doxycycline plus rifampin, streptomycin, or gentamycin. Fluoroquinolones plus rifampin, streptomycin, or gentamycin. TMP/SMZ less effective.
Q fever	Acute influenza-like illness, rare fulminant disease. High mortality due to endocarditis in predisposed patients. Liver function test (LFT) levations common.	Culture or animal inoculation (BSL-3) impractical. Serology widely available.	Macrolide, tetracycline, or fluoroquinolone for acute disease. Macrolide should be combined with rifampin if used for pneumonia. Doxycycline plus rifampin, chloroquine, or hydroxychloroquine if underlying valvular pathology.

Research and Reference Laboratories*

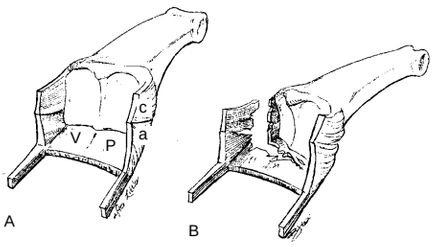
* **Initial contact and consultation, as well as specimen submission, is through state and local health departments. Phone numbers are available in the blue pages of the phone book or online listings at www.statepublichealth.org/directory.php or www.cdc.gov/other.htm or www.cdc.gov/ncidod/diseases/hanta/hps/noframes/statecon.htm.**

NAME	PHONE NUMBER	INTERNET
Centers for Disease Control and Prevention (CDC), Atlanta, GA	Tel: (770) 488-7100, (emergency response) (404) 639-1115 (special pathogens) or (404) 639-2888 (24 h)	www.bt.cdc.gov/ and www.cdc.gov/ncidod/dvbid/
Vector Borne Disease Laboratory, Fort Collins, CO	(970) 221-6400	
U.S. Army Medical Research Institute of Infectious Disease (USAMRIID), Fort Detrick, MD	(888)-872-7443	www.usamriid.army.mil

Emergency Medicine Reports
The Practical Journal for Emergency Physicians

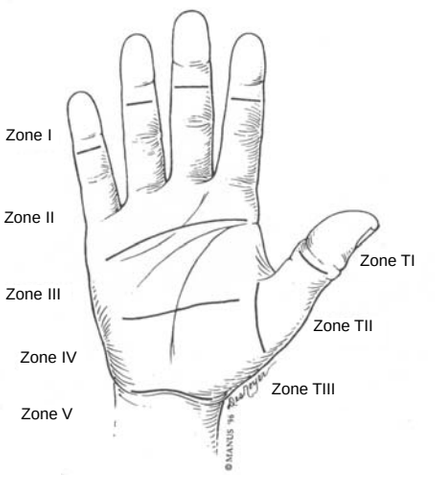
The Acute Hand, Part I

Close-up of Collateral Ligaments and Volar Plate



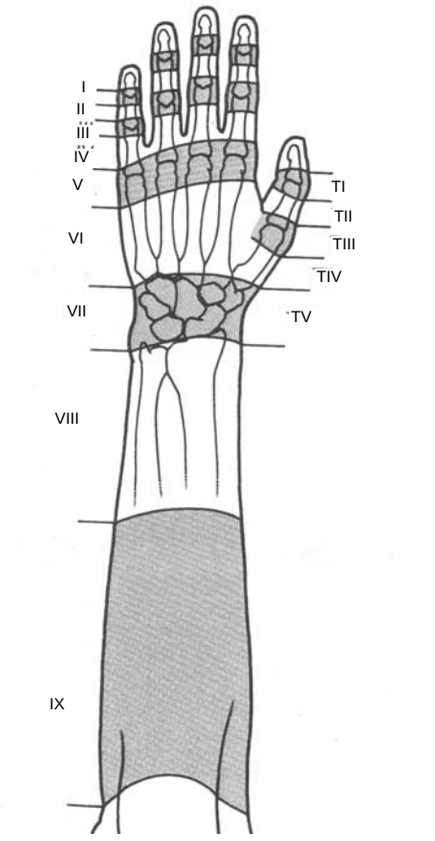
This diagram shows a close-up of collateral ligaments (a and c) and volar plate (VP) surrounding the finger joints. This box-like shape allows for maximum movement and stability of the joint. This figure shows how the ligaments and volar plate can be torn in dislocation.
Reprinted with permission: Rosen P, Barkin R, Hockberger R, et al., eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. St. Louis: Mosby;1999:638.

Zones of Flexor Tendons



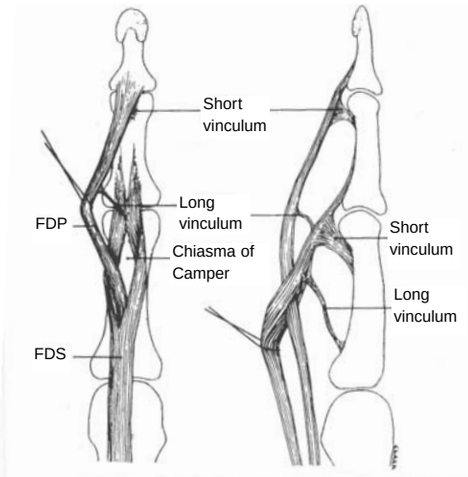
Reprinted with permission: Green DP. *Green's Operative Hand Surgery*, 4th ed. Philadelphia: Elsevier Science; 1999:1857.

Zones of Extensor Tendons



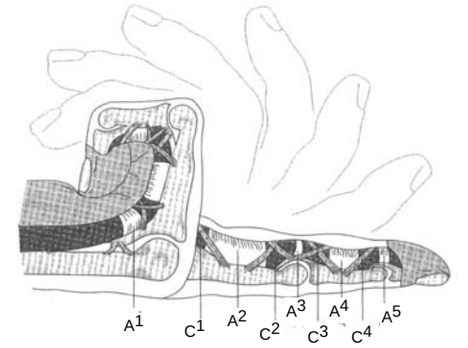
Reprinted with permission: Green DP. *Green's Operative Hand Surgery*, 4th ed. Philadelphia: Elsevier Science;1999:1956.

Insertions of Flexor Digitorum Superficialis and Flexor Digitorum Profundus Tendons in the Finger



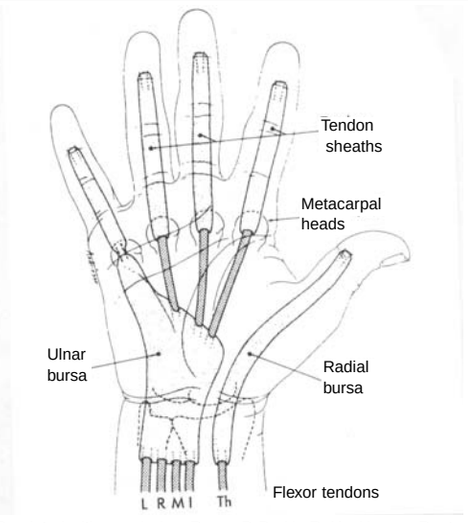
FDS = Flexor Digitorum Superficialis
FDP = Flexor Digitorum Profundus
Note that FDP becomes superficial to FDS in the proximal phalanx.
Reprinted with permission: Rosen P, Barkin R, Hockberger R, et. al, eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. St. Louis: Mosby; 1999:634.

Flexor Tendon Pulleys



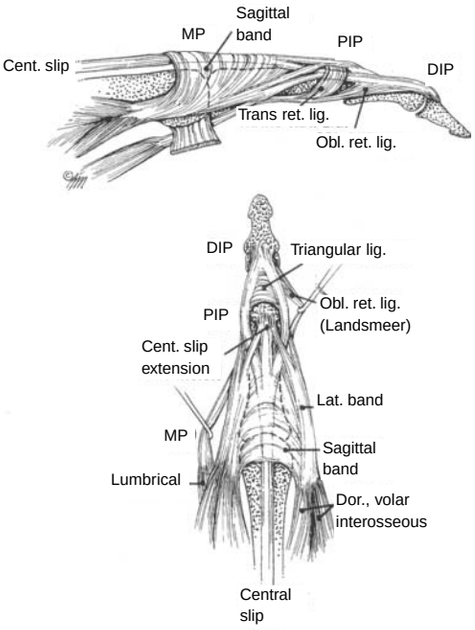
This drawing of the flexor tendon pulleys shows how they function to prevent bowstringing of the flexor tendon with finger flexion. The A2 and A4 pulleys are considered essential ones.
Reprinted with permission: Rosen P, Barkin R, Hockberger R, et al, eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. St. Louis: Mosby; 1999:634.

Flexor Tendon Sheaths and Bursae



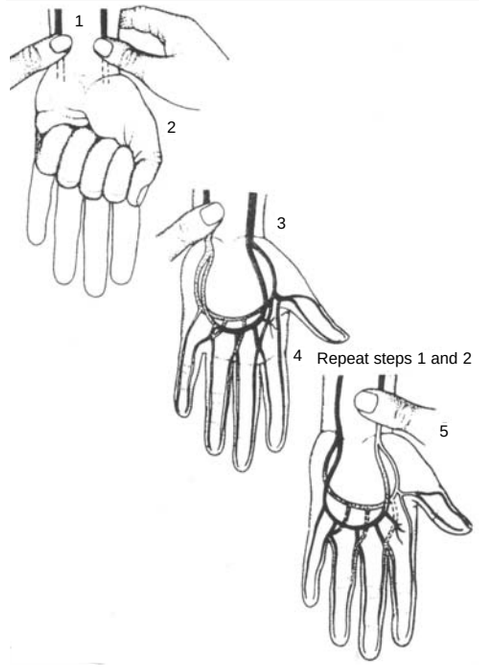
Reprinted with permission: Rosen P, Barkin R, Hockberger R, et. al, eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. St. Louis: Mosby;1999:635.

Insertions of Extensor Tendons in the Finger



This figure shows how complex the relationship is between the extensor tendon and its attachments in the finger.
Reprinted with permission: Rosen P, Barkin R, Hockberger R, et. al, eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice.* St. Louis: Mosby;1999:633.

The Allen Test



This figure shows the proper technique to perform the Allen test. In 1, both arteries are compressed. In 2, the hand is clenched and relaxed several times to empty it of blood. In 3, a single artery is released and blood flow to the fingers evaluated. A normal result is obtained when each artery alone can provide adequate blood flow to the hand. This also can be modified for testing patency of digital arteries.
Reprinted with permission: Rosen P, Barkin R, Hockberger R, et. al, eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice.* St. Louis: Mosby; 1999:637.

What Not to Do with an Acute Hand

- Do not make predictions about the care a consultant will provide (i.e., re-implantation) or about the outcome of treatment the patient will receive from another physician.
  - –The patient should receive the same message from all staff members caring for them (including nurses).
  - –Do not give the patient conflicting information.
- Always perform a full sensory exam before giving local anesthesia.
- If possible, involve consultants early in complex cases to allow them the opportunity to participate if they desire.
  - –This gives them "early warning" of a case that needs urgent attention from them and may accelerate care for the patient.
  - –It also avoids later complaints that something was not done to their specification.
- Call the re-implantation team or begin transportation arrangements immediately upon presentation of patient with obvious need for re-implantation.
  - –Do not wait for x-rays or any studies to be done.
  - –Cool amputated part appropriately to minimize warm ischemia time.
- Minimize repeat examinations of a painful hand as much as possible.
- DO NOT blindly clamp vessels.
- Always close lacerations of the hand when discharging the patient to see the consultant in the office, except in cases of infection, bite wounds, or if requested not to by the consultant.
- Keep patients who may be OR candidates NPO while in the ED.

Supplement to *Emergency Medicine Reports*, November 4, 2002: "The Acute Hand: Assessment and Management in the ED Setting. Part I: Anatomy, Assessment, and Initial Management." *Authors:* **Gary Hals, MD, PhD,** Attending Physician, Department of Emergency Medicine, Palmetto Richland Memorial Hospital, Columbia, SC.