

We have some information on early types of breast milk banks, and we thought it might be useful to supplement this with information from interested pediatric hospitals or neonatal units that have "new model" banks or are attempting to establish them. We would also welcome any advice or references about earlier models.

If any such groups or units wish to send their name and address to us, we will mail to them a short questionnaire on practices, procedures and problems. If there is sufficient response to the questionnaires we will analyse the results and make them available to correspondents and possibly a wider audience.

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### Reaction to intraperitoneal penicillin

*To the editor:* Various irrigating solutions are used during surgical operations for washing out the peritoneal cavity. While generally accepted as useful this practice may on occasion be dangerous. The use of antibiotic-containing fluids in particular may be the cause of iatrogenic disease, as the following case report demonstrates.

A 67-year-old woman was admitted to hospital following perforation of a left-sided colostomy as a consequence of a self-administered enema. Severe abdominal

pain had developed and had quickly become generalized.

She was in severe distress. Pulse rate was 90 beats/min, blood pressure was 140/100 mm Hg and temperature was 37°C. Generalized board-like rigidity of the abdomen, with diffuse guarding and tenderness, was detected. No masses were palpable.

That evening, under general anesthesia, laparotomy was performed. A perforation of the colostomy was repaired and the abdomen irrigated with a penicillin-streptomycin solution. The patient tolerated the procedure well. Prophylaxis with tetracycline, 350 mg/d given intramuscularly (IM), was also begun that day.

Postoperatively the patient had a low-grade fever (Fig. 1) and on the 7th post-operative day an erythematous, confluent, pruritic rash developed. It was believed that the patient was reacting to the tetracycline, so ampicillin, 500 mg IM *q6h*, was substituted. The next day the patient's temperature became even more elevated and the rash more confluent, erythematous and pruritic. The following day it was realized that the patient was likely reacting to the penicillin solution given intraperitoneally during the operation. Ampicillin was discontinued and the patient was given antihistaminics. By the next day there was some improvement of the rash, and a day later the rash had improved greatly and was no longer pruritic. Within 3 days the patient's temperature had returned to normal and the rash had completely disappeared. She made an uneventful recovery.

In this case the intraperitoneal penicillin was equivalent to injected drug. The patient reacted to the antibiotic, and the reaction was made worse by the ampicillin. Thus, caution is needed

in irrigating the peritoneal cavity with antibiotic-containing solutions.

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### *Pseudomonas cepacia* septic arthritis due to intra-articular injections of methylprednisolone

*To the editor:* *Pseudomonas cepacia* — *Pseudomonas multivorans* or *Pseudomonas kingii* (EO-1 [Eugonic Oxidizer, group 1]) — is a pleomorphic gram-negative bacillus that has been recovered with increasing frequency from hospitalized patients.<sup>1,2</sup> The organism is resistant to a number of commercial antiseptic agents used in hospitals, such as 0.15% N-dimethylbenzyl ammonium chloride in water and phenoxypolyethoxyethanol (Detergicide); 0.05% chlorhexidine; 0.5% cetrimide (Savlon); 1:5000 chlorhexidine (Hibitane); and pioloxidene and benzalkonium chloride (Resiguard). Each of these antiseptics has been associated with nosocomial infection.<sup>3,4</sup> We describe the course of a patient in whom septic arthritis due to *Pseudomonas cepacia* developed following intra-articular injections of a multidose preparation of methylprednisolone.

A 58-year-old healthy woman had complained of pain in the left ankle for several weeks. Her physician found the ankle to be tender but not swollen. On three separate occasions intra-articular injections of 20 mg of methylprednisolone acetate (Depo-Medrol) were given. Her condition improved, but 4 days before admission to hospital the pain increased. Radiographs and movements of the ankle were normal, and oral therapy with analgesics was prescribed.

On the day of admission, 10 days after the last injection of methylprednisolone, swelling of the medial aspect of the left ankle appeared. The patient was afebrile, had no other complaints and was comfortable at rest. She did not mention the injections. Her temperature was 36.7°C; blood pressure, 140/88 mm Hg; pulse rate, 68 beats/min; and respiration, 16/min. The only abnormality was the warm, swollen, tender, fluctuant left ankle. There was no radiographic evidence of osteomyelitis. The leukocyte count was  $8.6 \times 10^9/l$ , with 76% segmented neutrophils, 22% lymphocytes and 2% monocytes. Hematocrit, platelet count, results of urinalysis and of SMA-16 (including the uric acid value), chest radiograph and electrocardiogram were normal.

On the evening of admission, arthrocentesis yielded 3 ml of purulent fluid; Gram staining showed that it contained many leukocytes but no bacteria. With relief of pressure the pain lessened. The leukocyte count in the fluid was  $88 \times 10^9/l$ , with 98% polymorphonuclear cells and 2% lymphocytes; protein concentra-

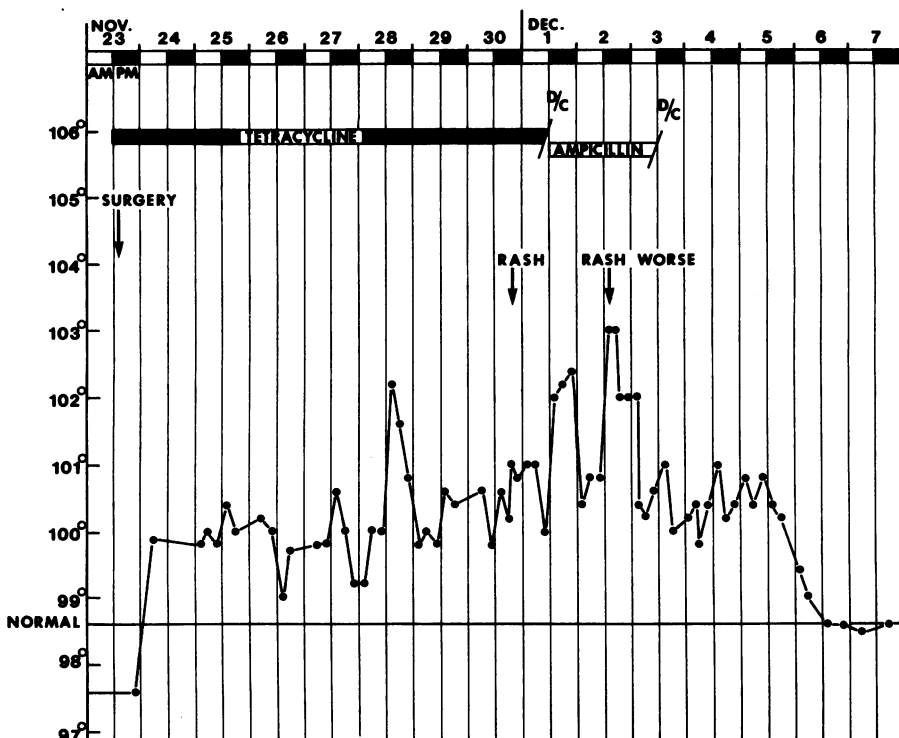


FIG. 1—Clinical course of reaction to intraperitoneal irrigation with penicillin.

tion was 3.5 g/dl and glucose concentration, 32 mg/dl. The blood glucose concentration was then 157 mg/dl. Mucin clotting was poor and rheumatoid factor was absent in serum and joint fluid. No uric acid or calcium pyrophosphate crystals could be seen in the joint fluid under polarized light. Synovial fluid, blood, urine and cervical smear were cultured.

The patient was allergic to penicillin and, since the history of injections of methylprednisolone remained undisclosed, therapy with clindamycin, 600 mg intravenously *q6h*, was begun. The next day, a second synovial tap yielded 5 ml of thick, cloudy fluid. Its leukocyte count was  $39 \times 10^9/l$ , with 98% polymorphonuclear cells; protein concentration was 4.7 g/dl and glucose concentration, 57 mg/dl (simultaneous blood glucose concentration, 125 mg/dl). The fluid was again cultured. By the 3rd hospital day the initial joint fluid culture had grown an aerobic gram-negative bacillus.

Clindamycin therapy was stopped and gentamicin, 80 mg intramuscularly *q8h* (4 mg/kg·d), begun. Blood, urine and cervical cultures remained negative.

The second synovial fluid culture revealed the same gram-negative bacillus. Isolates were susceptible to gentamicin, tobramycin, kanamycin and chloramphenicol, but resistant to ampicillin, carbenicillin, cephalothin, tetracycline and colistin. With Mueller-Hinton broth the minimum inhibitory concentration (MIC) of gentamicin was 0.25 µg/ml.

After the fifth intramuscular injection of gentamicin the route of administration was changed to intravenous. Slowly the ankle swelling decreased, and by the 6th day of appropriate treatment the ankle's range of motion had improved.

After 96 hours of gentamicin therapy the synovial fluid was serosanguinous and 2 hours and 45 minutes after the patient had received a dose it contained 9.5 µg/ml of gentamicin when the serum contained 12.0 µg/ml.<sup>5</sup> Culture of the fluid was sterile. On the 17th day of treatment some walking and physiotherapy was possible. Gentamicin therapy was continued for 33 days without renal or eighth nerve toxicity. Before the patient's discharge on the 35th hospital day there was no sign of osteomyelitis. At follow-up 3 months later she was completely recovered.

During the patient's 1st week in the hospital the attending physician's office was visited, and samples for culture were taken of xylocaine (Lidocaine; two vials), triamcinolone acetonide (Kenalog; four vials), swabs, alcohol, pads, thimerosal (Merthiolate), hexachlorophene (pHisb-Hex) and methylprednisolone (two vials). Cultures were sterile except for those of specimens from both multidose vials of methylprednisolone, which yielded 2000 and 3000 colonies/ml, respectively, of *Pseudomonas cepacia*.

The recovery of *Pseudomonas cepacia* from two separate aspirations of synovial fluid, as well as from two opened multidose vials of methylprednisolone that had been used for intra-articular injections of the ankle, establishes the mode of contamination in

this case. Corticosteroids are sometimes given intra-articularly to ameliorate a variety of painful inflammatory disorders of joints. The procedure is not innocuous and the danger of complicating septic arthritis has been noted.<sup>6</sup> To our knowledge, however, the special danger of aqueous suspensions of opened multidose preparations of any steroids, such as methylprednisolone, being a nutrient medium for a number of gram-negative bacilli including *Pseudomonas cepacia* has not been emphasized. The risk is likely the same as that for reservoir nebulizers, which have been used in inhalation therapy and have caused nosocomial epidemics.<sup>7</sup>

Patients with septic arthritis caused by gram-negative bacilli have not done well.<sup>5</sup> About 25% have died and survivors have commonly been crippled. Delays in beginning appropriate treatment sometimes have made amputation necessary.<sup>5,8</sup> Our patient recovered after repeated needle aspirations of the ankle joint and a 33-day course of gentamicin given parenterally. Determinations of gentamicin's MIC for *Pseudomonas cepacia* and its concentrations in serum and synovial fluid are necessary to ensure effective therapy of septic arthritis caused by gram-negative bacilli.

Infections associated with the use of multidose containers, particularly in the absence of an adequate preservative, are well known.<sup>9</sup> Organisms multiply after their introduction into solutions of medications.<sup>10</sup> Thus, if medications are to be injected into body cavities or spaces, single-dose preparations should be used.

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## References

1. EDERER GM, MATSEN JM: Colonization and infection with *Pseudomonas cepacia*. *J Infect Dis* 125: 613, 1972
2. MOODY M, YOUNG V, KENTON D: In vitro antibiotic susceptibility of pseudomonads other than *Pseudomonas aeruginosa* recovered from cancer patients. *Antimicrob Agents Chemother* 2: 344, 1972
3. BASSETT D, STOKES K, THOMAS W: Wound infection with *Pseudomonas multivorans*. A water-borne contaminant of disinfectant solutions. *Lancet* 1: 1188, 1970
4. HARDY PC, EDERER GM, MATSEN JM: Contamination of commercially packaged urinary catheter kits with pseudomonad EO-1. *N Engl J Med* 282: 33, 1970
5. GOLDENBERG D, BRANDT KD, CATHCART ES: Acute arthritis caused by gram-negative bacilli. A clinical characterization. *Medicine (Baltimore)* 53: 197, 1974
6. GOWANS J, GRANIERI P: Septic arthritis. Its relation to intra-articular injections of hydrocortisone acetate. *N Engl J Med* 261: 502, 1959

## HALOG CREAM

### Halcinonide 0.1%

Halog Cream (halcinonide, 0.1%) is intended for use as an anti-inflammatory agent for topical application. Halog Cream, 0.1%, provides 0.1% halcinonide, in a specially formulated water-washable base consisting of glyceryl monostearate, cetyl alcohol, myristyl stearate, isopropyl palmitate, polysorbate 60, and propylene glycol.

**ACTION:** Halog Cream, 0.1%, produces significant or complete therapeutic responses in patients with acute or chronic corticosteroid-responsive dermatoses.

**INDICATIONS:** Halog Cream, 0.1%, is indicated for topical application for relief of the many acute or chronic corticosteroid-responsive dermatoses.

**CONTRAINDICATIONS:** Tuberculous, fungal and most viral lesions of the skin (including herpes simplex, vaccinia and varicella).

Halog Cream is not intended for use in the eye nor in the external auditory canal of patients with perforated eardrums.

**WARNINGS:** Systemic side effects may occur and must be kept in mind particularly during use over large areas or for an extended period of time. Occasionally, symptoms of steroid withdrawal may develop when the medication is stopped after prolonged use.

**Pregnancy:** Safety has not been established. Potential benefit should be weighed against possible hazard.

**PRECAUTIONS:** If local infection (other than those cited in CONTRAINDICATIONS) exists, suitable concomitant antimicrobial therapy should be administered. If a favourable response does not occur promptly, application of the corticosteroid should be discontinued until the infection is adequately controlled by appropriate measures.

If local irritation or sensitization develops, halcinonide cream should be discontinued.

**Occlusive Dressing Technique:** The use of occlusive dressings increases the percutaneous absorption of corticosteroids and the possibility of systemic effects. For patients with extensive lesions it may be preferable to use a sequential approach. The patient should be kept under close observation during prolonged occlusive therapy.

Thermal homeostasis may be impaired if large areas of the body are occluded.

Occasionally, a patient may develop a sensitivity reaction to a particular occlusive dressing material or adhesive.

If infection develops, discontinue the use of the occlusive dressings and institute appropriate antimicrobial therapy.

**ADVERSE REACTIONS:** Significant local irritation is uncommon; a transient burning sensation may occur in some patients. The use of corticosteroids under occlusive dressings is known to produce miliaria, folliculitis, pyoderma, or localized cutaneous atrophy; striae occasionally develop. Erythema, dryness, itching and change in skin pigmentation have been reported with topical steroids.

### SYMPTOMS AND TREATMENT OF OVERDOSAGE:

Mild, reversible suppression of adrenal function, ecchymoses of the skin, peptic ulceration, hypertension, aggravation of infection, hirsutism, acne, edema and muscle weakness due to protein depletion are all toxic symptoms of corticosteroids. Animal studies suggest that overdosage may result in swollen breasts or lactation. Treatment is symptomatic; corticosteroid administration should be discontinued.

**DOSAGE AND ADMINISTRATION:** Usual adult dosage range: 2 to 3 applications daily.

**Occlusive Dressing Technique:** Gently rub a small amount of the Halog Cream, 0.1%, into the lesion until the cream disappears. Then re-apply the cream, leaving a thin coating on the lesion and cover with a pliable non-porous film. Good results have been obtained by applying Halog Cream, 0.1%, under occlusion in the evening and reapplying Halog Cream, 0.1%, without occlusion in the morning (i.e. — 12-hour occlusion). Reapplication of the preparation is essential at each dressing change.

**DOSAGE FORMS:** Halog Cream is supplied as cream formulation containing 0.1% halcinonide, in tubes of 15, 30 and 60 g.

**STORAGE:** Store at room temperature. Avoid freezing. Avoid prolonged storage at temperatures exceeding 30°C.

*Product monograph available to physicians and pharmacists on request.*

**References:** 1. Data on file, Squibb Institute of Medical Research. 2. Sudilovsky A, Clewe TH: *J Clin Pharmacol* 15:779-784, 1975. 3. Clark RF, Clement ER: *Arch Dermatol* 111:731-733, 1975.



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**VELOSEF 250 CAPSULES**  
**VELOSEF 500 CAPSULES**  
**Cephadrine Capsules**

**VELOSEF 125 FOR ORAL SUSPENSION**  
**VELOSEF 250 FOR ORAL SUSPENSION**  
**Cephadrine for Oral Suspension**

**VELOSEF FOR INJECTION, 500 mg and 1.0 g**  
**Cephadrine for Injection**

**ACTION:** Cephadrine is a semi-synthetic, cephalosporin antibiotic exhibiting bactericidal activity through inhibition of cell-wall synthesis.

**INDICATIONS:** Infections in the respiratory and genitourinary tracts, and in the skin and soft tissues, due to susceptible organisms.

Sensitivity tests should be performed; therapy may be instituted before receiving the results.

**CONTRAINDICATIONS:** Hypersensitivity to the cephalosporin group of antibiotics.

**WARNINGS:** There is evidence of partial cross-allergenicity between the penicillins and the cephalosporins. Therefore, cephadrine should be used with caution in patients with known hypersensitivity to penicillins.

Antibiotics, including cephadrine, should be used cautiously and only when absolutely necessary in patients with a history of allergies, particularly to drugs.

**Usage during pregnancy and lactation:**

Safety for use of this product during pregnancy has not been established. Cephadrine is secreted in breast milk.

**PRECAUTIONS:** Patients should be observed carefully during therapy. Allergic reactions require discontinuation of VELOSEF and appropriate treatment.

Prolonged use of VELOSEF may result in overgrowth of non-susceptible organisms; appropriate measures should be instituted. During long-term therapy, hematology, renal and hepatic functions should be monitored periodically. Patients with known or suspected renal impairment should be observed carefully since cephadrine may accumulate in the serum and tissues unless dosage is suitably reduced. See DOSAGE AND ADMINISTRATION section.

Indicated surgical procedures should be performed in conjunction with antibiotic therapy; e.g., the incision and drainage of abscesses. After treatment with cephalosporins, a false-positive reaction for glucose in the urine may occur, but not with enzyme-based tests. A false-positive Coombs' test has also been reported.

VELOSEF for Injection is physically compatible with most commonly used intravenous fluids and electrolyte solutions (e.g. Dextrose Injection, Sodium Chloride Injection or M/6 Sodium Lactate). However, it is not compatible with Lactated Ringer's Solution or other calcium-containing infusion fluids.

**ADVERSE REACTIONS:** Usually limited to gastrointestinal disturbances and occasional hypersensitivity, but may include hematological and hepatobiliary disturbances, as well as elevated BUN, LDH and serum creatinine, superinfection, vaginitis and joint pains. Thrombophlebitis following I.V. injection and sterile abscesses after I.M. injection have occurred.

Only occasionally have adverse reactions been severe enough to warrant cessation of therapy.

**DOSEAGE AND ADMINISTRATION:** The presence of food in the gastrointestinal tract delays absorption and reduces the peak serum level but does not affect the total amount of cephadrine absorbed.

VELOSEF Capsules and VELOSEF for Oral Suspension.

Adults: Respiratory tract infections: 250 mg, q6h or 500 mg q12h.

Pneumococcal lobar pneumonia: 500 mg, q6h or 1 g q12h.

Genitourinary tract infections: 500 mg, q6h or 1 g q12h. Prolonged therapy is advisable for the treatment of prostatitis and epididymitis.

Skin or soft tissue infections: 250 mg q6h or 500 mg q12h.

Children: 25 to 50 mg/kg/day, in two or four equally divided and spaced doses, e.g.:

**VELOSEF for Oral Suspension**

Child's Weight	125 mg/5 ml	250 mg/5 ml
10 kg (22 lbs)	½ to 1 tsp. q6h or 1 to 2 tsp. q12h	—
20 kg (44 lbs)	1 to 2 tsp. q6h or 2 to 4 tsp. q12h	½ to 1 tsp. q6h or 1 to 2 tsp. q12h
40 kg (88 lbs)	—	1 to 2 tsp. q6h or 2 to 4 tsp. q12h

Smaller doses than those indicated above should not be used.

For otitis media due to *H. influenzae*, doses from 75 to 100 mg/kg/day are recommended.

Maximum daily dose should not exceed 4 g.

VELOSEF for Injection: For use in moderate, severe or life threatening infections or where oral therapy is not possible. Adult daily dose range is 2 - 4 g, depending on the infection. In children, a daily dose of 50 - 100 mg/kg is recommended.

**All patients, all formulations:**

Larger doses (up to 1 g q6h in adults or up to 25 mg/kg q6h in children) may be given for severe or chronic infections; maximum daily dose should not exceed 4 g. Therapy should be continued for a minimum of 48 to 72 hours after the patient becomes asymptomatic or evidence of bacterial eradication has been obtained. In infections caused by hemolytic streptococci, a minimum 10-day-treatment period is recommended. Stubborn infections may require treatment for several weeks with frequent bacteriological and clinical appraisal.

A modified dosage schedule in patients with decreased renal function is necessary. Each patient should be considered individually; the following schedule is recommended as a guideline. Initial loading dose: 750 mg. Maintenance dose: 500 mg at the time intervals listed below:

Creatinine Clearance (ml/min/1.73m <sup>2</sup> )	Time Interval
> 20 ml/min	6 - 12 hours
15-19 ml/min	12 - 24 hours
10-14 ml/min	24 - 40 hours
5-9 ml/min	40 - 50 hours
< 5 ml/min	50 - 70 hours

**DOSEAGE FORMS:** Capsules of 250 mg and 500 mg in bottles of 50, and bottles of VELOSEF 125 and 250 for Oral Suspension which, after reconstitution, provide 100 ml of a pleasantly flavoured suspension containing 25 mg/ml and 50 mg/ml respectively.

VELOSEF for Injection is provided as a sterile powder for reconstitution in vials containing 500 mg or 1.0 g. Consult Product Monograph or Package insert for reconstitution procedure.

Product Monograph available to physicians and pharmacists on request.

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7. REINARZ JA, PIERCE AK, MAYS BB, et al: The potential role of inhalation therapy equipment in nosocomial pulmonary infection. *J Clin Invest* 44: 831, 1965  
 8. TINDEL J, CROWDER J: Septic arthritis due to *Pseudomonas aeruginosa*. *JAMA* 218: 559, 1971  
 9. SYKES G: *Disinfection and Sterilization*, 2nd ed, Philadelphia, Lippincott, 1965, p 449  
 10. SPALTER J, JACKSON M, MATZ R: Bacteria in medications. Growth during emergency resuscitation. *NY State J Med* 76: 693, 1976

**IgD myeloma: a case report**

*To the editor:* Several syndromes that include hypogammaglobulinemia have been described; each is characterized by an increased susceptibility to infection. They are divided into primary and secondary immunodeficiency diseases.<sup>1</sup> The former are hereditary and idiopathic, whereas the latter may result from various disorders involving the reticuloendothelial system.

In the cases of spontaneous fractures and bone pain, a neoplastic disease is suspected. If the erythrocyte sedimentation rate (ESR) is low and the heat test for Bence Jones protein is negative, a diagnosis of multiple myeloma may be difficult to make. The case reported below was first investigated as one of neoplastic disease.

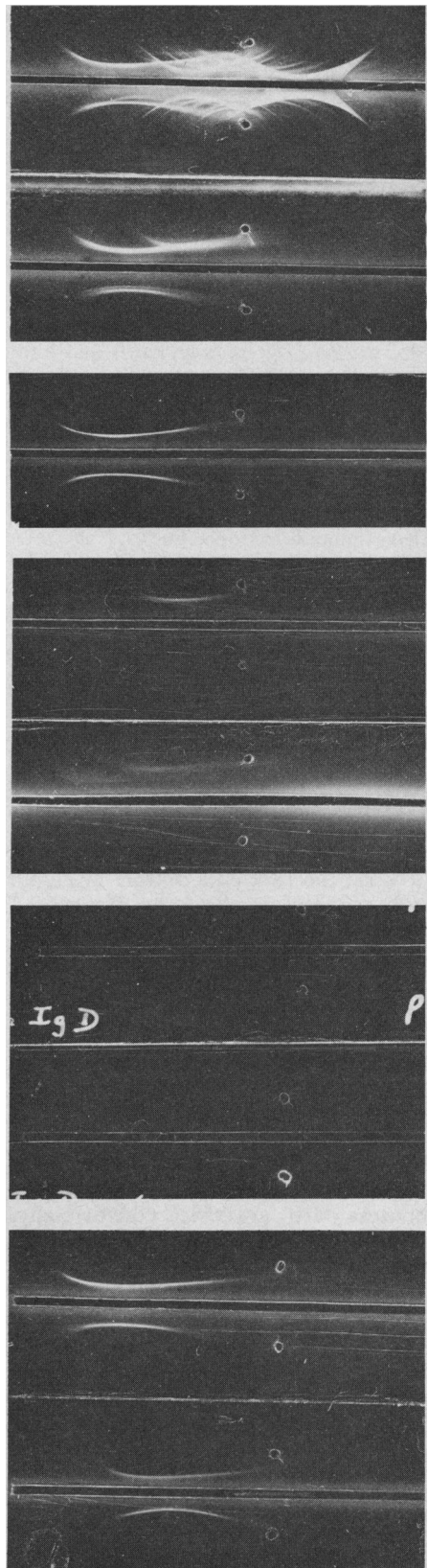
A 71-year-old woman was admitted to hospital with chest and back pain of 3 weeks' duration. Because of inability to walk and dyspnea she was bedridden. Physical findings were unremarkable except for small stature and dorsal kyphosis.

Three years previously she had sustained a traumatic fracture of the right clavicle. The sternum was painful on pressure. Diffuse osteoporosis was noted on radiographs from a metastatic survey.

Hemoglobin value was 11.8 g/dl; total



**FIG. 1—Osteolytic lesions compatible with metastases or multiple myeloma.**



**FIG. 2—Results of immunoelectrophoresis of normal human serum (upper panel of each pair) and patient's serum (lower panel) with the following antisera, reading from top to bottom: polyvalent antiserum, anti-immunoglobulins, anti-IgG, anti-IgA, anti-IgM, anti-IgD, anti-IgD with patient's serum concentrated fourfold, anti-κ and anti-λ. Patient's serum shows abnormal results on testing with anti-D with serum concentrated fourfold, and with anti-λ.**