

Fatal *Pseudomonas* Septicemias in Burned Patients *

KEHL MARKLEY, M.D.,† GABRIEL GURMENDI, M.D., PABLO MORI CHAVEZ, M.D.,
AUGUSTO BAZAN, M.D.

Lima, Peru

DURING THE COURSE of the Peru Burn Project⁷ one of the major difficulties encountered was a high late mortality, especially in burned children. In all parts of the world late deaths after burns are still a major complication in which the role of infection has been prominent,¹⁻⁶ but in Peru this problem has been especially serious because of the high incidence of fatal *Pseudomonas* (*B. pyocyaneus*) septicemias. During the last five years evidence has been accumulating in the literature that the incidence of *Pseudomonas* infections is increasing with the greater use of a wide variety of antibiotic therapy,⁴⁻¹⁰ and more and more authors are beginning to believe that *Pseudomonas aeruginosa* can be pathogenic under certain conditions.^{5, 6} Jackson, Lowbury and Topley have reported five deaths due to *Pseudomonas aeruginosa* infections in burned patients treated in England.⁴

Quite frequently associated with the *Pseudomonas* septicemia seen in Peru was a characteristic skin lesion appearing in the non-burned area. Although there has been little written about such a lesion in *Pseudomonas* infections, Frankel, in 1917, described skin lesions associated with pyocyaneus infection,² and more recently Gepfert *et al.*³ and Mirabel⁸ have reported skin lesions in infants and children suffering from pyocyaneus infections with infantile diarrhea.

It is the purpose of this communication to report our experience in Peru with this

fatal complication as a major cause of late deaths in burned children and adults.

CLINICOPATHOLOGIC STUDY

During the past four and one-half years in Peru a total of 172 children and 103 adults have been studied with burns involving 10 per cent or more of the body surface. In this group of patients 29 burned children and three burned adults developed cutaneous lesions in the non-burned area associated with a *Pseudomonas* septicemia.

The lesions were usually of two types, but occasionally there were patients with both types at the same time. The more common type occurred in 72 per cent of the children with cutaneous lesions and appeared usually on the third to eighth day after thermal injury, although on rare occasions it was first observed between the eighth and forty-third day after burning (Table 1). The lesion began as a vesicle filled with an opalescent liquid and surrounded by an erythematous base. The vesicle broke rapidly and developed a cen-

TABLE 1. *Time of Appearance of Skin Lesions after Burning*

Type of Lesion	No. of Cases	Days after Burning				
		3-7 #	8-14 #	15-21 #	22-28 #	28-68 #
Children						
Necrotic	20	14	4	1	0	1
Subcut.	9	6	1	0	2	0
Adults						
Necrotic	3	1	1	0	0	1
Subcut.	0					

= number of cases.

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† Surgeon, U. S. Public Health Service, Department of Health, Education, and Welfare, National Institutes of Health, National Institute of Arthritis and Metabolic Diseases, Bethesda, Md.

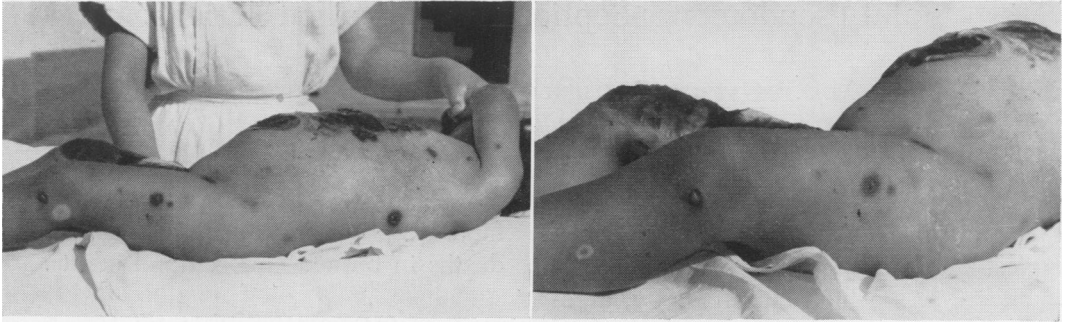


FIG. 1. The photographs illustrate the characteristic, superficial, necrotic type of cutaneous lesions occurring in the non-burned areas in a child with a *Pseudomonas septicemia*.

tral area of necrosis, while the erythematous base changed to a purple-red color and became quite hard. The initial vesicle was followed in rapid succession by the appearance of multiple lesions similar to the first one in other parts of the body not burned (Fig. 1). Only one patient was seen with two such lesions in the burned area. No lesions were found on mucous membranes or soles or palms. Generally death occurred in 24 to 48 hours after the appearance of the first vesicular lesion.

The second type occurred in 28 per cent of the patients with cutaneous lesions. It appeared at any time from the fifth to twenty-eighth day after burning in the non-burned areas as a subcutaneous nodule, usually painful to touch, accompanied by a slight redness of the overlying skin. Usually there were several such nodules present, but the number was always much less than that seen with the superficial, necrotic type. These patients, for the most part, deteriorated less rapidly, but died two to 12 days after the appearance of the first nodule.

Similar clinical pictures were associated with both types of cutaneous lesions. With the advent of the skin lesion, the burned area itself was covered either by bluish-green pus or by a thick, black crust. The patient had fever up to 39° C., great thirst, marked abdominal distention and depression of the central nervous system. Death was preceded by a state of coma, subnor-

mal body temperatures, rapid and shallow respiration and progressive circulatory failure which led to death in shock.

Laboratory analyses demonstrated anemia and hypoproteinemia in every case. Usually the leucocyte count was within the normal range, but if the course was rapidly fatal, there was leucopenia, or if the course was prolonged before death, there was leucocytosis. Differential counts always showed a marked increase of non-segmented leucocytes. Almost always there was evidence of hyponatremia, hyperkalemia, and metabolic acidosis.

At autopsy, 34 burned patients presented characteristic lesions in the viscera. Their gross appearance varied from petechial-like hemorrhages on the surfaces of the pleura and pericardium to large isolated or confluent infarctions of a blackish-red color in the lungs or kidneys (Fig. 2). Usually the focal area of hemorrhage had a central part of greyish color, sometimes undergoing liquefaction due to necrosis. Lesions in the lungs and kidneys were quite numerous and extensive, while much less numerous in liver, heart and intestines. The localization of the visceral lesions is demonstrated in Table 2.

Microscopic examination of the cutaneous lesions showed marked hydropic degeneration and vacuolization of the epithelial cells with vesicle formation. In certain sections of the cutis and subcutis, edema, hemorrhage and necrosis were encoun-

TABLE 2. Localization of Visceral Lesions in Deaths Due to *Pseudomonas*

Site of Visceral Lesion	% of Cases with Visceral Lesion in this Site
Lungs	97
Kidneys	74
Heart	24
Intestines	15
Liver	9

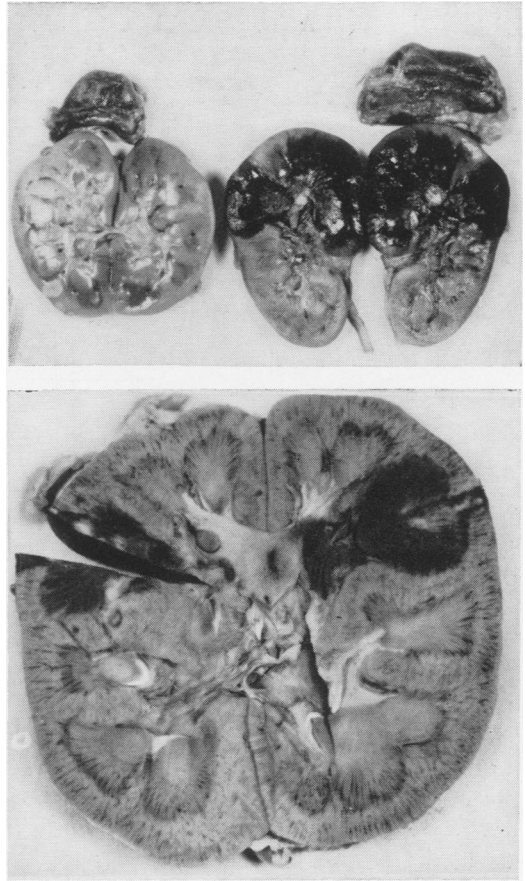


FIG. 2. The photographs demonstrate the typical visceral lesions observed in the kidney in burned patients with a *Pseudomonas* septicemia.

tered. There was marked basophilia of the tissues in the necrotic zone, while at the periphery of this area could be found slight evidence of leucocytic infiltration. The blood vessels of the surrounding area were dilated and in the walls of these vessels could be demonstrated gram-negative rods (Fig. 3). The visceral lesions also showed hemorrhage, necrosis and slight leucocytic infiltration.

BACTERIOLOGIC STUDY

One or more blood cultures were drawn, using all of the customary sterile precautions, from veins in areas that were free from burns in 25 of the 29 burned children with skin lesions and in all of the three burned adults with skin lesions. The results of these cultures are summarized in table 3.

Of the total group only three children had cultures negative for *Pseud. aeruginosa*. One of these cases was a child in which a single blood culture was drawn two days before the appearance of the cutaneous lesion, and the other two were cases in which a single blood culture was drawn on the

day of the appearance of the subcutaneous nodular type of lesion where death did not occur until five to 12 days later.

Cultures of the biopsies of the cutaneous lesions in five cases, of the vesicular fluid in one case and of the urine in one case

TABLE 3. Incidence of *Pseudomonas* Septicemia in Patients with Skin Lesions

Age Group	No. with Skin Lesions	No. with Blood Cultures	Blood Cultures Positive for				Blood Cultures Negative	
			Pseudo. Alone		Pseudo. + Others		#	%
			#	%	#	%		
Children	29	25	21	84	1	4	3	12
Adults	3	3	3	100	0	0	0	0

= number of cases.

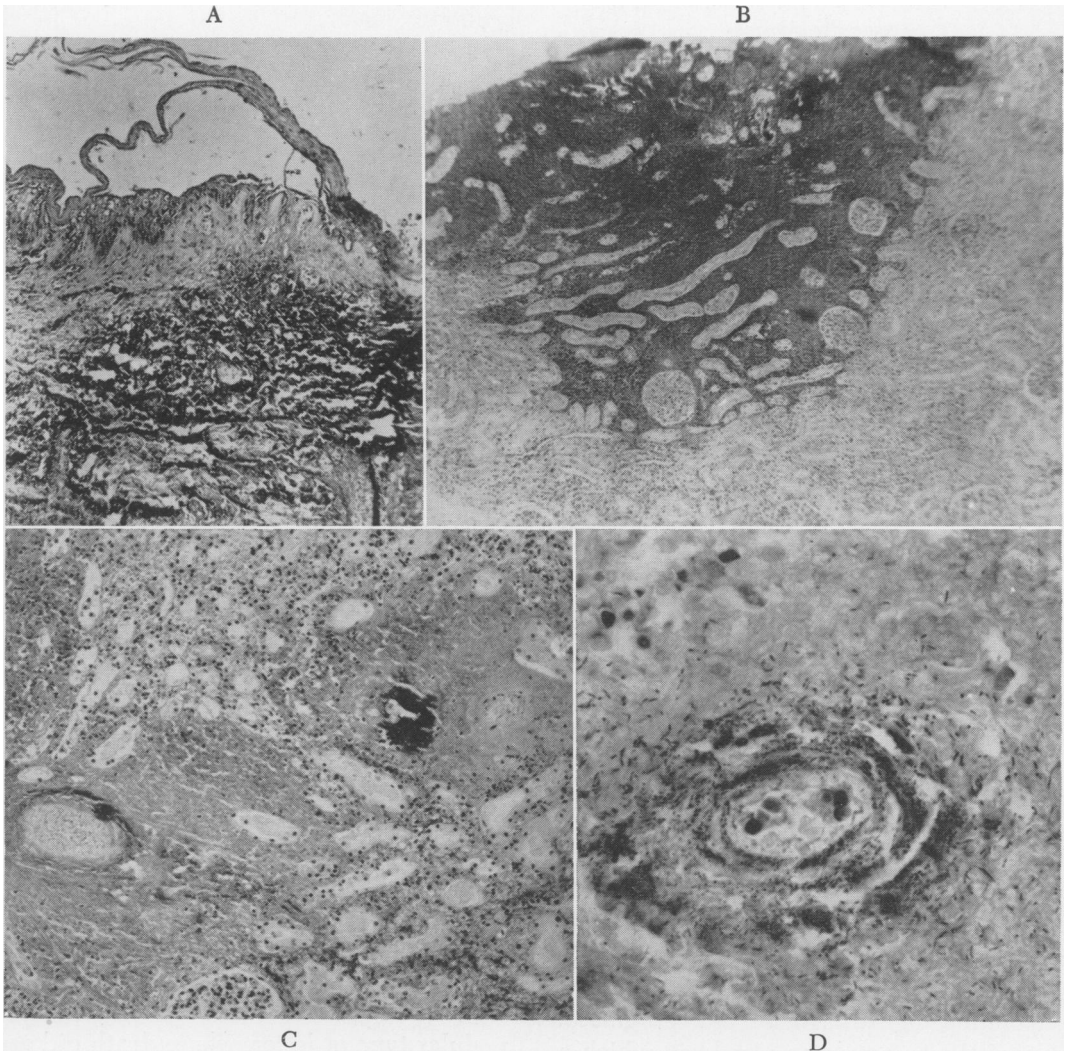


FIG. 3. The photomicrographs illustrate: A—a section of the cutaneous lesion at low magnification showing vesicle formation; B—section of the kidney at low magnification demonstrating a small triangular area of infarction; C—section of kidney at higher magnification showing thrombosed vessels surrounded by areas of necrosis with slight leucocytic infiltration at the margins; D—section of subdermis at high magnification stained especially to demonstrate the gram-negative rods in the blood vessel wall and its surrounding stroma.

with cutaneous lesions all grew *Pseud. aeruginosa*. In 14 cases cultures of the burned area were done with all of them positive for *Pseud. aeruginosa* together with a variety of other organisms, including *non-hemolytic Staphylococcus*, *Escherichia coli*, *Aerobacter aerogenes*, and pathogenic *Staphylococcus albus*. At autopsy, cultures of pulmonary lesions in two cases and of

renal lesions in one case demonstrated positive cultures of *Pseud. aeruginosa*.

All blood, skin and visceral biopsies were grown in bacto-tryptose broth (Difco®) to which had been added penicillinase (Schenley), and produced colonies of *Pseudomonas* on bactotryptose agar (Difco®) that contained a greenish-yellow pigment which could be extracted in chloroform.

TABLE 4. *The Incidence of Pseudomonas Septicemias in Late Burn Deaths*

Group	No. of Cases	No. of Cases with Blood Culture	Blood Cultures Positive for				Blood Cultures Negative	
			Pseudo. Alone		Pseudo. + Others		#	%
			#	%	#	%		
Children†								
Infection period with death	20	18	17	94	0	0	1	6
Infection period without death	36	7	0	0	0	0	7	100
Shock period	62	9	0	0	0	0	9	100
Adults‡								
Infection period with death	32	11	7	64	2	18	2	18
Infection period without death	63	12	0	0	0	0	12	100

† Covering the period from August, 1954 to January, 1956.

‡ Covering the period from July, 1951 to January, 1956.

= number of cases.

The infection period with death represents the total number of burned patients who died at some time after the first 48-hour post-burn period and in whom the blood cultures were taken on the last two days before death. The infection period without death represents the total number of burned patients who were eventually discharged well from the hospital and in whom blood cultures were taken during the period 3-14 days post-burn. The shock period represents the total number of burned patients in whom blood cultures were taken during the first 48-hour period after burning.

Three separate cultures of *Pseud. aeruginosa* isolated from the blood and cutaneous lesions of a child who died of this infection were all of the same serologic type: 10:1,2.* These organisms were not sensitive to tetracycline in any concentration in vitro but were sensitive to Polymixin B® at concentrations above 30 micrograms/ml. of broth. Intraperitoneal and intravenous injection of 12×10^8 organisms, isolated from blood and cutaneous lesions, into normal mice, guinea pigs and rabbits killed all animals within 24 hours.

Not all of the patients who died from *Pseudomonas* septicemias, however, developed cutaneous or visceral lesions. In 28 burned individuals with positive blood cul-

tures for *Pseudomonas*, who came to autopsy between 1951 and 1956, only 78 per cent presented such lesions. Because of this fact, any study of incidence would necessarily demand the routine study of blood cultures in all patients. Table 4 presents the data to show the importance of this septicemia, especially in children, as the cause of almost all late deaths from burns in Peru.

THERAPY

All of the burned patients were cared for in an open, general surgical ward.** The routine prophylactic antibiotic therapy administered during the first two weeks after thermal injury consisted of crystalline penicillin G given via the intramuscular route

* We wish to thank Dr. Elizabeth Verder of the National Institutes of Health for typing these organisms. Details of the ten serologic types⁹ are to be published.

** Cutaneous lesions typical of a *Pseud.* septicemia appeared only in burned patients on the ward and never in other surgical cases.

TABLE 5. Treatment Administered for *Pseudomonas* Septicemia.

Age Group	No. of Cases	Pen. #	Oxy-tetra. #	Tetra. #	Poly. #	Tetra. + Poly. #	Oxy-tetra. + Poly. #	Eryth. + Poly. #	Sulfa IV #
Children	19	1	1	4	3	7	1	1	1
Adults	7	5	0	1	0	0	0	0	1

= number of cases.

Dosage schedules: Penicillin, 100,000 units 4 times daily in children and 100,000 units intramuscularly every 3 hours in adults; Oxytetracycline, 125 mg. per os every 6 hours; Tetracycline, 50 mg. intramuscularly 3 times daily in children and 100 mg. per os every 6 hours in adults; Polymixin B, 5.0 mg./Kg. intramuscularly in divided doses; Tetracycline, 50 mg. intramuscularly 2 times daily and Polymixin B 5.0 mg./Kg. intramuscularly in divided doses; Sulfadiazine 1.8 Gm., Sulfathiazole 1.8 Gm. and Sulfamerazine 1.2 Gm. intravenously, Erythromycin 100 mg. per os 4 times daily and Polymixin B@ 5.0 mg./Kg. intramuscularly in divided doses.

in dosage of 50,000 units every six hours to children and 100,000 units every three hours to adults. Local treatment of the burn consisted of the exposure method with the application of a sulfanilamide preparation called "Prontyl"® in the children, whereas the exposure method with no local chemotherapy or antibiotic therapy prevailed during the same time in adults. Five to ten days after thermal injury the burn was covered with vaseline gauze and dry dressings in both children and adults. The treatment instituted at the first indication of a pyocyanus infection, either by the appearance of cutaneous lesions or by a positive blood culture, is indicated in Table 5:

As of the present date of writing, no effective therapy has been found to prevent death in the patients with *Pseudomonas* septicemias. Since therapy, once the skin lesions have appeared, has been of no avail, an attempt is being made to prevent the septicemia by the prophylactic administration of Polymixin B® after the patient has passed the first 48-hour period. The results of this study will be reported at some future date.

SUMMARY

During the course of the Peru Burn Project, in which 172 children and 103 adults with burns involving 10 per cent or more of the body surface have been studied, it

has been demonstrated that *Pseudomonas aeruginosa* septicemias have been the major cause of death occurring after the initial 48-hour post-burn period. Multiple, characteristic vesicular or nodular cutaneous lesions appeared in the non-burned areas in 78 per cent of the burned children with positive blood cultures for *Pseudomonas*. At autopsy, multiple hemorrhagic and necrotic lesions from which *Pseudomonas* could be cultured were found in the viscera. No effective antibiotic or chemotherapeutic agent has been discovered as yet to prevent death of these patients.

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