

MEDICAL GRAND ROUNDS
Parkland Memorial Hospital
September 17, 1964

Gram-Negative Rod Bacteremia

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VII. Summary

CASE #1: [REDACTED]

The patient was a 59-year-old N [REDACTED] female admitted on [REDACTED]/57 because of a chronic varicose ulcer on the right leg. Admission physical examination was essentially unremarkable except for the varicose ulcer. Blood pressure 180/110. The admission laboratory studies included hemoglobin 11.8, white count 5,400, and occasional WBCs in the urine. Chest film was unremarkable. Because of the pyuria, the patient was placed on gantrisin 2 gm. loading dose followed by 1 gm. every 6 hours. The following day she suddenly developed a temperature of 102° and arthralgia in the elbows, wrists, knees and back. The following day she complained of stiffness of the neck. Two lumbar punctures were within normal limits. The gantrisin was continued through [REDACTED], during which time she spiked daily temperatures to 102°. On [REDACTED], penicillin and streptomycin were added to the regimen with no apparent effect. The initial urine culture was sterile. Repeat white count on [REDACTED] was 10,300. The admission BUN was 11. Blood culture drawn on [REDACTED] was apparently contaminated, inasmuch as two different organisms were isolated from each bottle and subsequent blood cultures were negative. Electrocardiogram revealed left ventricular strain or digitalis effect.

On [REDACTED]/57, the patient's blood pressure dropped to 95/55. It was felt that she most likely had gram-negative rod bacteremia and she was begun on a regimen including neomycin 0.5 gm. intramuscularly daily, hydrocortisone 300 mg. daily, chlorpromazine 100 mg. daily, and 4 ampoules of Levophed per liter. Repeat studies revealed a BUN of 64 mg.%, CO₂ 16, Na 126. Urine output was approximately 5-10 cc. per hour. On [REDACTED], she developed a gallop rhythm and on [REDACTED]/57, died. Post-mortem examination revealed acute diffuse interstitial non-suppurative nephritis compatible with gantrisin hypersensitivity, and a diffuse generalized interstitial myocarditis.

CASE #2: [REDACTED]

The patient was a 62-year-old [REDACTED] female admitted for the last time in [REDACTED] 1959. Her present illness apparently began in [REDACTED] 1959, when she was brought to the emergency room in a confused, stuporous state with a history of fever. On admission she was found to have a temperature of 105°, blood pressure 120/60, pulse 108, respirations 56. Physical findings included obesity and the stuporous state. Blood studies included serum Na of 137 and a serum potassium which fell to 2.9 mEq/L. Electrocardiograms revealed no evidence of myocardial infarction and an EEG was normal. On admission the patient was started on streptomycin, chloramphenicol, and was given intravenous hydrocortisone. Her blood pressure subsequently rose, but Aramine was required for the next few days for the maintenance of normotensive levels and prednisolone (20 mg. daily) was continued for the next 6 days. The patient became afebrile after the first hospital day. Studies including chest film, GI series, were normal. Barium enema revealed sigmoid diverticulosis. Her leucocyte count remained normal throughout. Three blood cultures and a urine culture were sterile. After 2 weeks of hospitalization she was discharged.

In [REDACTED] 1959 she again became disoriented and confused and 1 day prior to her admission ([REDACTED]/59) she noted chills, fever and vomiting. Physical examination revealed blood pressure 70/0, temperature 104.6°, pulse 96, respirations 35. She was again confused and her physical was otherwise unchanged from previously. She was immediately placed on Levophed, chloramphenicol, streptomycin, intravenous hydrocortisone and intravenous fluids. Twenty-four hours after admission, the patient became afebrile and

oriented, although her blood pressure required some Levophed for 3 days. She was placed on KCl supplementation and the hydrocortisone continued for 7 days. Again, numerous blood and urine cultures were sterile. Electrocardiograms revealed no evidence of infarction. On [REDACTED] and again on [REDACTED], the patient had transient hypotensive episodes associated with vomiting but no fever. Her blood pressure stabilized without steroids or vasopressor agents on the first occasion, but hydrocortisone was given on the second occasion. On [REDACTED] the patient complained of abdominal pain, nausea and vomiting, with a normal blood pressure and temperature. She was felt to have an incarcerated incisional hernia and was taken to surgery. Before an incision was made, the patient became hypotensive and required vasopressors and hydrocortisone. A gangrenous loop of terminal ileum was found. Post-operatively she was maintained on intravenous and intramuscular hydrocortisone for 12 days. On [REDACTED], the patient suddenly spiked a temperature of 103° and her blood pressure disappeared.

Post-mortem examination revealed bilateral destruction of the adrenal glands with acid-fast organisms being demonstrable.

Comment: This patient represents the difficulty in making the diagnosis of gram-negative rod bacteremia with shock. Based upon the clinical diagnosis, she had been treated with steroids and brought out of adrenal insufficiency on at least 3 occasions prior to her fatal episode.

CASE #3: [REDACTED]

The patient was a 60-year-old [REDACTED] female admitted on [REDACTED], 1958, with the history of being in good health until 4 days prior to admission, when she developed a frank shaking chill, became nauseated and vomited. Subsequently she noted dull aching lower abdominal pain. She developed anorexia. She became progressively weaker and on the morning of admission became confused. Admission physical examination revealed blood pressure 60/40, pulse 138, respirations 30. She was a disoriented Negro female with skin revealing decreased turgor. The skin was dry and warm. Admission laboratory studies included hemoglobin 11.3, white count 3,600 with 76% neutrophils. Urinalysis revealed 30-50 WBC. Blood urea nitrogen 28, CO₂ 18.7. She received 4000 cc. of Ringer's lactate intravenously, which improved her skin turgor but urine output remained 12 cc. per hour and her blood pressure remained in the range of 80/50. Blood cultures were drawn and she was placed on tetracycline. Her hemoglobin fell to 7 gm.% and white count rose to 17,000, with 85% neutrophils. Six hours after admission the patient was taken to the operating room and under local anesthesia a mass in the left flank was explored and aspirated. This contained 400 cc. of infected urine associated with a large hydro-nephrotic kidney. Within 12 hours post-operatively her blood pressure had returned to 115/65 and remained at that level. Urine flow increased with a urine output of 2100 cc. the first 24 hours post-operatively. Subsequently a blood culture revealed *E. coli*, as did the pus and the urine. The organism was sensitive to tetracycline, chloramphenicol, streptomycin, neomycin and polymyxin B. Subsequently she was treated with streptomycin, chloramphenicol. On the 18th hospital day, a left nephrectomy was performed and the patient has subsequently done well.

Comment: This patient illustrates the importance of drainage of infected foci in the management of gram-negative rod bacteremia.

CASE #4: [REDACTED]

The patient was a 54-year-old [REDACTED] male who was readmitted on [REDACTED] 1964.

Present illness: The patient had a cerebrovascular accident 2 years earlier with a residual left-sided hemiplegia. He apparently was doing satisfactorily until [REDACTED] 64, when he was found to be unresponsive and unable to speak. The following day he developed cough and fever. He was seen by his local physician, who told his wife that the patient had had another stroke and "double pneumonia".

Physical examination revealed blood pressure 114/90, pulse 110, respirations 26, temperature 103°. The patient was well-developed but unresponsive except to painful stimuli. Neurologic examination revealed evidence of a right hemiplegia, aphasia, as well as the old left spastic hemiparesis. Laboratory studies included hemoglobin 15.4, white count 12,400 with 67% polys. Urinalysis revealed specific gravity 1.034 and 0-3 white cells. Six blood cultures drawn at admission were negative. Sputum culture revealed Diplococcus pneumoniae and some proteus. Urine culture on admission was sterile. Initial therapy included electrolytes, tetracycline. Inasmuch as urine outputs were recorded, apparently a Foley catheter had been inserted. Chest x-rays revealed stranding on the left, most compatible with aspiration pneumonitis. The patient became afebrile by [REDACTED] and seemed to be doing satisfactorily until [REDACTED] 64, when he had a frank shaking chill. With this episode, the patient's blood pressure decreased from approximately 150/100 to 90/50. Urine output for 8 hours was 600 cc. Blood cultures were drawn and the patient was begun on kanamycin and colistin. He was begun on Aramine, which was continued slowly until [REDACTED]. With discontinuation of the Aramine, his blood pressure dropped to 80/50 but responded without additional vasopressor. Urine culture obtained on [REDACTED] revealed greater than 100,000 Proteus mirabilis, sensitive to kanamycin and chloramphenicol. Two blood cultures revealed the same organism with essentially the same sensitivity, although some inhibition with colistimethate was noted. The patient subsequently did satisfactorily and ultimately had a feeding jejunostomy. He was discharged to a nursing home.

Comment: This patient represents an example of probable hospital-acquired gram-negative urinary tract infection with bacteremia. His hypotension was only of modest degree and the patient responded satisfactorily to very small doses of vasopressor agents. Adrenocortical steroids were not administered.

CASE #5: [REDACTED]

This was the first [REDACTED] admission for this 70-year-old [REDACTED] female who was transferred from an alcoholic sanitarium because of fever and coma of 24 hours' duration. She apparently had received Librium for sedation 48 hours prior to admission. At the time of her admission to the emergency room, her blood pressure was unobtainable, temperature 104.6°. She immediately received intravenous fluids which contained 5 ampoules of Levophed and 500 mg. of hydrocortisone hemisuccinate by intravenous push. Upon admission to the ward, her blood pressure was 110/0, pulse 140, respirations 24 and temperature 104.6°. Chest revealed coarse breath sounds and rhonchi over both bases. The liver and spleen were palpable. The bladder was distended to the umbilicus. Skin was cold and cyanotic. Initial hemoglobin was 14.7 gm.%, white count 15,800 with 89% neutrophils and a marked left shift. Urinalysis revealed the urine to be loaded with

white cells. BUN 32 mg.%, CO₂ 22, SGOT 170, bilirubin 0.7, and serum amylase 493. Serum phosphorus reported as 3.4 mg.%. Admission urine specimen revealed greater than 100,000 E. coli, which were sensitive to tetracycline, chloramphenicol and kanamycin. Two blood cultures were obtained which revealed E. coli with the same sensitivity pattern. Electrocardiogram revealed supraventricular tachycardia. The patient's blood pressure generally was maintained in the range of 100-110 systolic. She was placed on kanamycin and colistimethate. Urine output the first 24 hours was 2400 ml. Despite the return of her blood pressure and the administration of large doses of adrenocortical steroids, she required increasing amounts of Levophed to maintain her blood pressure and by [REDACTED] was requiring 20 ampoules of Levophed. She apparently vomited dark blood and died 30 hours after admission.

Comment: This patient received both large doses of adrenocortical steroids and vasopressor agents as well as appropriate antibiotics, but failed to respond. She failed to demonstrate increasing sensitivity to vasopressor agents as a result of glucocorticoid therapy.

Table 2
Cumulative Age-Specific Mortality (%)
(Excluding 1971)

Age Group	0-5	6-15	16-35	36-55	56-75	76-95	100+
Males	13	1	5	3	1	12	21
Females	7	0	16	21	12	5	36
Total	20	1	19	24	23	17	57
Shock	—	0	0	—	13	6	36
Mortality, %	13	100	21	36	13	21	36

Mortality - Age 16-35 years = 26% - 35 years = 36% p = 0.14
Males 5% Females 36% - 1971

Table 1

ETIOLOGIC CLASSIFICATION OF SHOCK

1. HYPOVOLEMIA
Hemorrhage, dehydration, loss of protein
2. CARDIAC FAILURE
Myocardial infarction, cardiac dysrhythmia
3. HYPERSENSITIVITY
Anaphylaxis, reaction to drugs
4. BACTEREMIA
Bacterial toxins (endotoxin)
5. NEUROGENIC
Vasomotor paralysis, spinal shock, ganglionic blockade
6. IMPEDIMENT TO BLOOD FLOW
Pulmonary embolism, dissecting aneurysm
7. ENDOCRINE FAILURE
Adrenal cortex, adrenal medullary hormones

Table 2

GRAM-NEGATIVE ROD BACTEREMIA - PMH
(Age-Mortality)

Age (yrs.)	0-5	6-15	16-35	36-55	56-75	> 75	Total (%)
Males	13	1	3	3	12	12	44
Females	7	0	16	11	17	5	56
Total	20	1	19	14	29	17	100
Shock	—	0	6	7	18	6	46
Mortality (%)	15	100	21	36	69	71	45

Mortality - Age 16-55 years - 26% > 55 years - 70% p < 0.001
Males 55% Females 39% N.S.S.

Table 3

GRAM-NEGATIVE ROD BACTEREMIA - PMH
(Shock)

Severity	80-89	70-79	50-69	< 50	Total
Number	20	5	7	6	38
Died	12	4	6	6	74%
Mortality (%)	60	89 p = 0.05			
Duration (hrs.)	< 12	12-24	25-36	37-48	> 48
Number	13	9	0	3	11
Mortality (%)	77	50 N.S.S.			73

Table 4

GRAM NEGATIVE ROD BACTEREMIA - PMH
(Site and Source of Infection)

Site of primary infection		Mortality	
Urinary tract infection	39%	44%	
Other sites		50%	
Source of acquisition		Shock	Mortality
Hospital-acquired	45%	47%	55%
Non-hospital acquired		25%	38%
			p = 0.05

Table 5

GRAM-NEGATIVE ROD BACTEREMIA - PMH
(Clinical and Laboratory Features)

Fever	< 99°	99-101°	101-103°	> 103°	
% patients	11	19	24	46	
Oliguria	50-500 cc/day		< 50 cc/day		
# patients	14		4		
% mortality	79		75		
WBC (1000's)	< 5	5-15	15-25	> 25	
% patients	16	58	18	8	
CO ₂ (mEq/L)	< 10	10-15	15-20	20-28	> 28
% patients	10	18	24	42	7
mortality - patients > 55 yrs.	without acidosis 45%				
	with acidosis 84% p < 0.05				

Table 6

GRAM-NEGATIVE ROD BACTEREMIA - PMH
(Bacterial Species)

Patients in Shock	
Pure culture	28
Mixed - Gm- and Gm-	7
Gm- and Gm+	2
Bacterial Species	
E. coli	19
A. aerogenes	11
Pseudomonas sp.	5
Proteus sp.	4
Others	6

Table 7

GRAM NEGATIVE ROD BACTEREMIA - PMH
(Therapy)

Antibiotics	Number of Patients	Mortality (%)	
Entire Group			
"Appropriate" antibiotics	65	42	
"Inappropriate" antibiotics	35	63	p < 0.02
Patients in Shock			
"Appropriate" antibiotics	26	62	
"Inappropriate" antibiotics	12	67	

Table 8

GRAM-NEGATIVE ROD BACTEREMIA - PMH
(In Vitro Antibiotic Sensitivities)

<u>Antibiotic Agent</u>	<u>% "Sensitive" in vitro (93)</u>
Penicillin G	1
Tetracycline	54
Streptomycin	61
Chloramphenicol	81
Kanamycin	89
Colistimethate	87

Table 9

GRAM-NEGATIVE ROD BACTEREMIA - PMH
(Therapy)

Adrenocortical Steroids	Entire Series		Shock Series	
	No. pts.	Mortality (%)	No. pts.	Mortality (%)
Steroids	18	67	15	87
No steroids	82	38	22	63
		p < 0.05		N.S.S.
Vasopressor Agents	23	78	—	—
Vasopressors	77	35	15	60
No vasopressor				

Table 10

GLUCOCORTICOIDS IN THERAPY OF SHOCK ASSOCIATED WITH
GRAM-NEGATIVE ROD BACTEREMIA

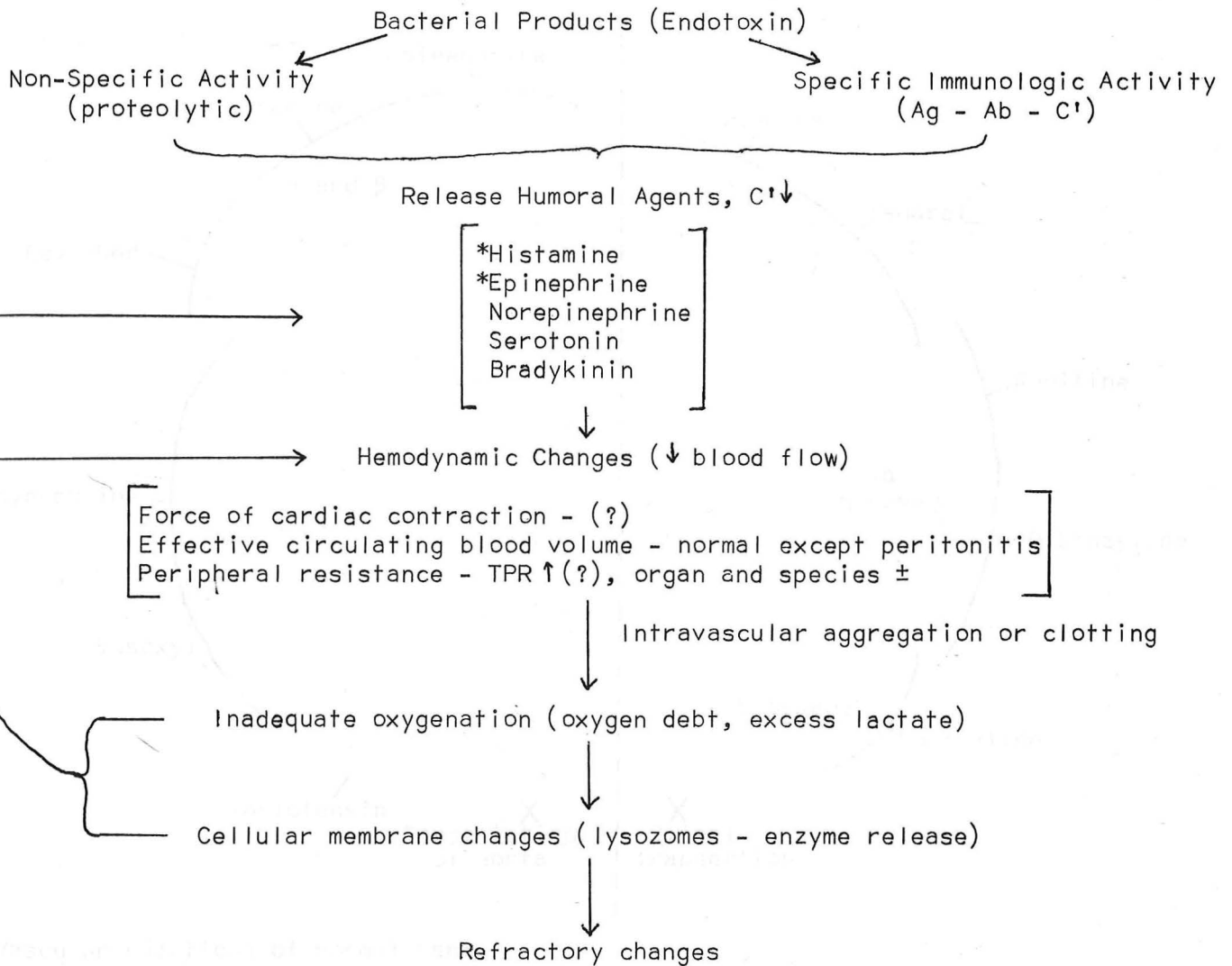
Author	None		Low Dosage (< 300)*		High Dosage (> 300)*	
	No. pts.	Mortality (%)	No. pts.	Mortality (%)	No. pts.	Mortality (%)
McCabe	108	26	** 40	63		
Weil	84	83	55	85	** 30	57
Reddin and Spink	—	—	25	72	** 7	27
PMH - 63-64	22	63	3	66	12	83
Total	214	51	123	75	49	59
					N.S.S.	

* mg./day

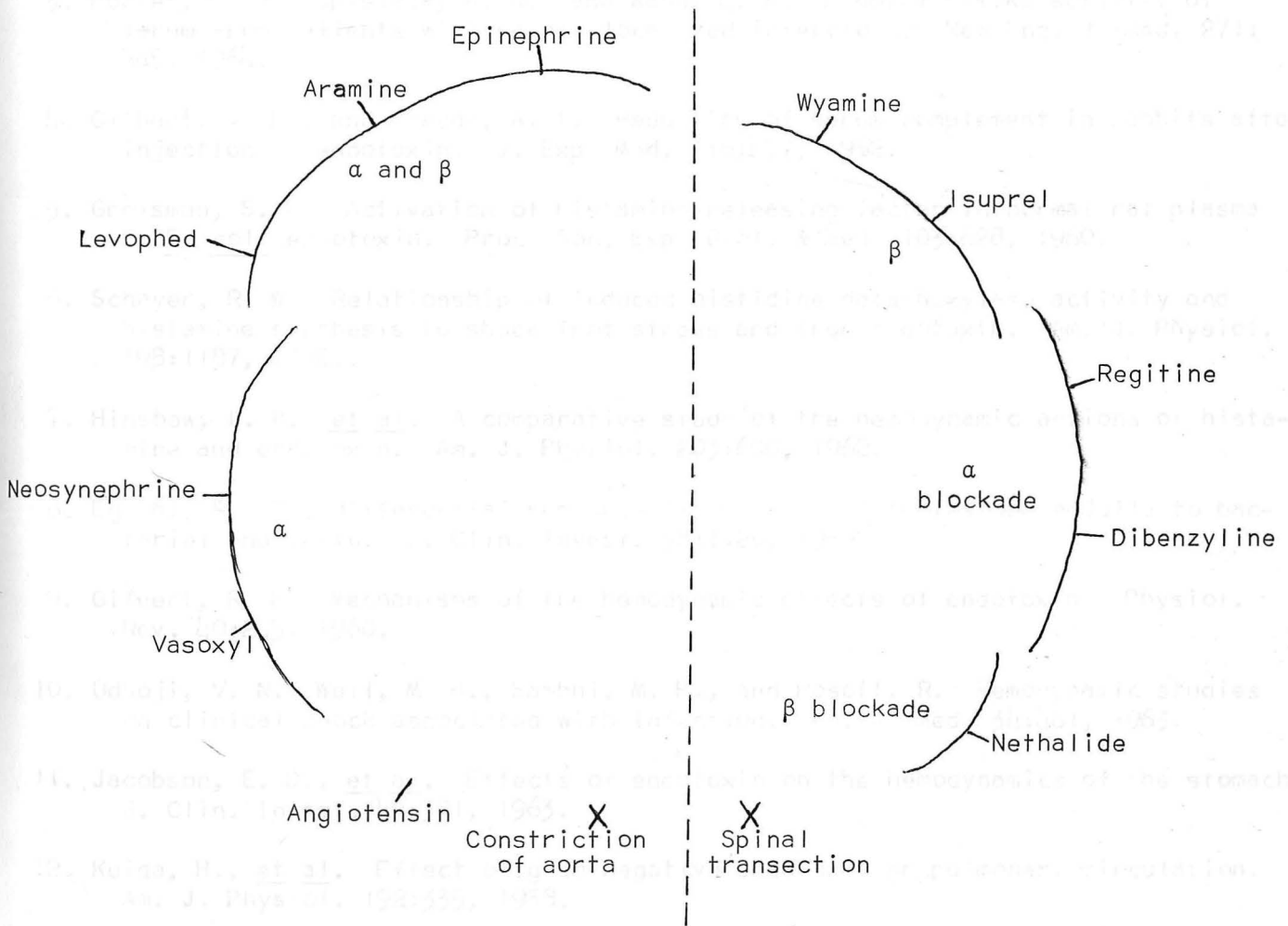
** Differences statistically significant at $p \leq 0.05$

Figure 1

PATHOGENESIS OF SHOCK ASSOCIATED WITH
GRAM-NEGATIVE ROD BACTEREMIA - HYPOTHESIS



ADRENERGIC ACTIONS (VASCULAR) OF SYMPATHOMIMETIC AGENTS (Schematization)



Vascular reactions of normal man:

- α receptors - \uparrow BP, \downarrow pulse
- β receptors - \downarrow BP, \uparrow pulse

-Adapted from Weil

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