

HYDROGEN ION CONCENTRATION IN EXUDATES OF PNEUMOCOCCUS INFECTION

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Lord (1, 2) has reported that exudates of pneumococcus infection show hydrogen ion concentrations greater than the blood serum by comparative measurement. With the dialysis method he was usually able to demonstrate acidity of marked degree in pneumonic sputum, empyema pus, and in exudates taken at autopsy from the solidified lungs of fatal cases of lobar pneumonia and from those of dogs with experimental pneumococcus pneumonia. In confirmation of Lord's observations, Takahashi (3) showed with electrometric methods that in pneumococcus empyema, the hydrogen ion concentration of the pus becomes progressively increased from approximately pH 7.00 at the onset, to values as great as pH 5.71 in the later stages. Takahashi found in addition that the empyema pus contained only 0.05 to 0.02 per cent of sugar.

Physicochemical changes in inflammation were first described by Opie (4) who titrated a decrease in alkalinity of exudates from the pleural cavities of dogs previously injected with irritants. Lord (1, 2), Koldajew (5), Gollnow (6), and Menkin (7) have with different methods found acidity in exudates from infections due to a variety of bacteria. By further studies of inflammation, Kempner (8) has shown that in the fluid of cantharides skin blisters, carbonic and lactic acids become increased in concentration with the aggregation of leucocytes, while the base and sugar are proportionately diminished in comparison with the blood. Light from another angle has been thrown upon the origin of these physicochemical changes by Menkin (9) and others. From the injection of dyes, the latter workers have adduced evidence to indicate that in focal inflammation, capillary permeability is increased, whereas diffusion from the lesion into the surrounding tissues and blood stream is reduced by the coagulation of fibrin and plasma in the capillaries and lymphatics. Thus, it appears that localized inflammation generally is characterized by an accumulation of acids with a corresponding depletion of base and

sugar, which proceeds from the metabolic activities of leucocytes, or leucocytes and bacteria, in an environment partly isolated from the rest of the body.

This paper is a report of observations on the hydrogen ion and sugar concentrations in exudates of pneumococcus infection. The exudates were obtained from the solidified lungs of dogs with pneumonia and from dermal infection in rabbits produced experimentally with the pneumococcus. Whereas Lord (1, 2) examined exudates secured post mortem, our materials were collected with biopsy methods in an effort to determine more nearly the range of hydrogen ion and sugar concentrations which occur within these lesions *in vivo*. In this way we have sought to compare the magnitude of the physicochemical changes within these primary infections with those described by Takahashi (3) in secondary empyema due to the pneumococcus.

Materials and Methods

Pneumonic Exudate.—Pneumonia was produced in normal dogs with a highly virulent strain of Type I Pneumococcus after the method of Terrell and Robertson (10). The course of the infection was followed with temperature readings, leucocyte counts, blood cultures, and x-ray examinations. Animals given artificial pneumothorax, received injections of 250 to 300 cc. of air over the affected lung at 20 to 24 hours and again at 32 to 36 hours. At stated intervals after inoculation, the animals were given 20.0 to 25.0 mg. per kilo of body weight of sodium amyral intravenously and a biopsy was then done. Through an incision across the costal cartilages, a consolidated lobe was excised and blotted dry of blood escaping from the open vessels. The pneumonic exudate was expressed from openings in the distal pleural surface and collected in cold dry dishes.

Exudate from Dermal Pneumococcus Infection.—Dermal infection was produced in large normal rabbits with highly virulent Type I pneumococci by the technic of Goodner (11). At given intervals during the course of the infection, fluid for examination was aspirated from the lesions with syringe and needle.

pH Determinations.—Specimens of exudate were covered with oil and kept on ice until the pH measurements could be completed. Determinations on the pneumonic exudate¹ from dogs were made electrometrically with a glass electrode known to be accurate to 0.10 of absolute pH and within 0.05 pH between different readings. Determinations on the exudate from dermal infection in rabbits were made with platinum electrodes and quinhydrone with approximately the same accuracy.

Sugar Determination.—On specimens of blood and exudate collected simultane-

¹ Kindness of Dr. T. Coolidge of the Department of Biochemistry.

ously, sugar determinations were done in duplicate by the micro method of Hagedorn-Jansen with cotton filters.

Pneumonic Exudate from Dogs

The course of the pneumococcus pneumonia in typical instances in dogs of these experiments is shown for reference in Chart 1. It can be seen that the infections were severe with bacteremia as a rule.

It is noteworthy that the exudate expressed from the pneumonic

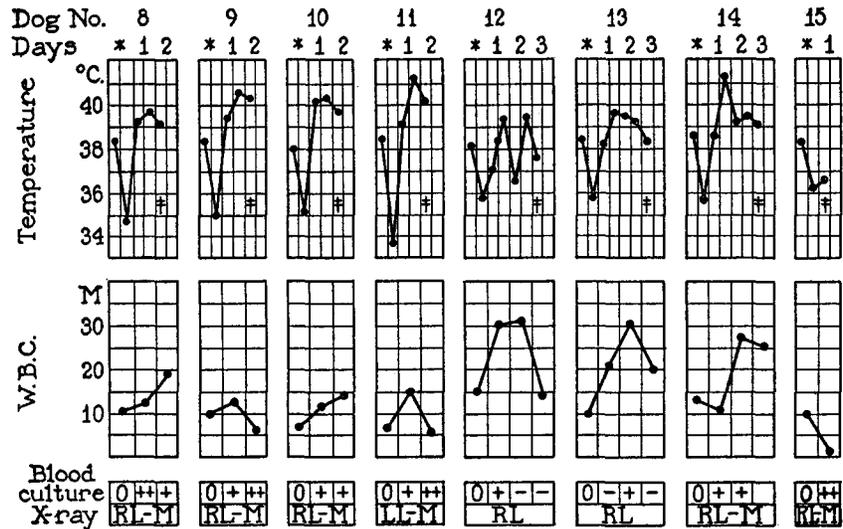


CHART 1. - = negative. + = 10 colonies or less per cc. ++ = more than 10 colonies per cc. 0 = not done.

RL-M = right lower and middle lobes, etc.

* Average normal temperature and the drop which followed morphine and sodium amytal anesthesia.

† Biopsy.

lungs of dogs was of viscid, mucosanguinous character with little fluid and a high content of fibrin and cellular materials comprised largely of phagocytes and erythrocytes in various states of preservation. The exudates also contained pneumococci in numbers between 6 hundred thousand and 8 million per cc. as determined from cultures of serial dilutions.

The results of the hydrogen ion and sugar determinations upon pneumonic exudate from fourteen dogs are presented in relation to

the duration of the infection and the general condition of the animals at the time, in Table I. The findings on the exudate from four dogs which received artificial pneumothorax are combined by reason of their similarity with those on the exudate from untreated animals. Included also for comparison are the results of sugar determination on the pneumonic exudate and blood from three animals which had died of the infection.

TABLE I

The Hydrogen Ion and Sugar Concentrations in Exudate from the Consolidated Lungs of Dogs with Experimental Pneumonia

Dog No.	Condition of animal	Duration of infection <i>hrs.</i>	pH of exudate	Sugar		Sugar deficit in exudate <i>per cent</i>
				Blood <i>mg. per cent</i>	Exudate <i>mg. per cent</i>	
4	Moderately ill	36	—	178-184	72-80	58.1
6	“ “	48	6.80	152-153	81-81	46.5
8	Severely “	42	7.15	124-130	56-60	54.3
11	“ “	48	6.75	86-93	43-54	44.8
12	Recovering	64	7.16	127-134	110-116	13.4
14	Extremely ill	66	6.73	66-74	47-53	28.5
15	“ “	16	7.18	54-60	17-24	64.0
5*	Severely “	48	—	63-72	74-74	+9.6
7*	“ “	36	7.07	102-106	105-110	+3.3
9*	“ “	44	6.75	101-103	91-95	8.8
10*	“ “	40	6.75	129-133	86-93	31.6
1	Dead, 15 min.	44	—	54-58	36-41	31.2
2	“ 30 “	30	—	50-57	26-32	56.5
3	“ 4-6 hrs.	24	—	38-43	15-20	32.0

— = not done.

* Artificial pneumothorax therapy.

The hydrogen ion concentration of the exudate from three of six untreated animals and from three others which received artificial pneumothorax was definitely greater than is found in the blood of living dogs. The pH of the exudates from three untreated animals approached the lower limits of normal for the blood. The pH of the exudates varied between 7.18 and 6.73 and bore no apparent relationship to the duration of the infection, or to the general condition of the animals employed in the experiments.

The sugar content of the pneumonic exudate was significantly lower than that of the blood in all dogs except three of the four dogs treated with artificial pneumothorax, in which the values for exudates and blood were practically equal. Parallel to the observations of Lord (1, 2) upon the increase of acidity in pneumonic exudates taken at autopsy, the sugar concentrations were below normal in the blood and still further reduced in the exudates from animals which had died of the infection. Difference in sugar content between the exudate and blood could not be correlated with the pH of the exudate, the duration of the infection, or the condition of the animal in the experiments. Blood sugar levels in living animals were high or low depending upon

TABLE II
The Hydrogen Ion and Sugar Concentrations in Exudate from Dermal Pneumococcus Infection in Rabbits

Rabbit No.	Condition of animal	Duration of infection	pH of exudate	Sugar		Sugar deficit in exudate
				Blood	Exudate	
		<i>hrs.</i>		<i>mg. per cent</i>	<i>mg. per cent</i>	<i>per cent</i>
4	Moderately ill	18	6.80	131-140	67-72	47.8
5	“ “	18	6.76	105-112	33-42	65.4
	Extremely “	30	6.66	83-88	51-60	35.1
6	Moribund	30	6.78	39-48	9-15	72.4
7	Moderately ill	36	6.87	120-129	80-85	33.4
	“ “	60	6.81	112-112	40-45	62.0

whether or not they had been too ill to eat the food which was freely provided for all.

Exudates from Dermal Infection in Rabbits

As an example of practically non-sanguinous exudate from a primary pneumococcus infection, the serous fluid aspirated from typical lesions of dermal infection in rabbits was examined with the results given in Table II.

It can be seen that the hydrogen ion concentration of the exudate from the dermal infection was regularly increased beyond values found in the blood of living rabbits. Likewise, the sugar content of

the exudate was in each instance considerably lower than that of the blood. However, the hydrogen ion concentration of the exudate which varies between pH 6.87 and 6.66, was not always proportional to the difference in sugar content between the exudate and blood under the condition of our experiments.

SUMMARY

The hydrogen ion concentration in the lesions of experimental pneumococcus infection has been estimated directly by pH determinations on exudates from living animals. For indirect evidence of an increase in hydrogen ion concentration within the lesions, the difference in sugar content between exudate and blood from animals with pneumococcus infection has been measured.

With sanguinous exudate from the consolidated lungs of dogs with experimental pneumococcus pneumonia, the findings were not always consistent, but usually there was either direct or indirect evidence of increased hydrogen ion concentration. The physicochemical changes in exudate from animals treated with artificial pneumothorax showed no important differences from those in other specimens. In concurrence with Lord's (1, 2) observation of increased acidity in pneumonia exudate obtained at autopsy, sugar concentrations, which are low in the blood, were markedly reduced in exudates from animals which had died of the infection.

Serous exudates from dermal pneumococcus infection in rabbits uniformly showed definite acidity by both direct and indirect methods of estimation. The hydrogen ion concentrations in exudate from dermal pneumococcus infection in rabbits varied between pH 6.87 and 6.66 but were not always proportional to the difference in sugar concentrations between the exudate and blood. While these hydrogen ion concentrations are similar to those attained in the pneumonic exudate from dogs, they are of lesser magnitude than those which Takahashi (3) has described in the pus of secondary empyema due to the pneumococcus.

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