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HEMORRHAGE IN EPIDEMIC INFLUENZA.

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In the recent influenza epidemic which has swept through the land from coast to coast and invaded the Military Hospitals with such intensity, there has been one factor of clinical evidence almost constantly present.

Early in the course of the epidemic at Camp Dodge Base Hospital, the attention of the Head Surgery Service was called to a violent, persistent and remarkably frequent epistaxis that seemed to occur almost as a prodrome, or as an early symptom in the course of the attack. Patients admitted to the hospital invariably complained of a fullness in the head, and on inspection the mucosa of the upper respiratory tract, especially involving the nose, naso-pharynx and fauces, presented a diffusely congested, slightly swollen and dark-red injected appearance. The site of this epistaxis was invariably in the septal mucous membrane, along the course of the septal artery and about the center of the quadrilateral cartilage. An occasional exception in this point of hemorrhage was found in the junction of the septum and the floor of the nose. In some fifteen or sixteen cases where the hemorrhage was observed promptly and bacteriological service was immediately available, blood cultures were made from this septal point during the epistaxis, and in five of these cases the definite presence of streptococcus hemoly-

ticus was demonstrated. This was, perhaps, the earliest evidence of the presence of this specific micro-organism in blood cultures during the epidemic.

Over one hundred and fifty cases of this type of epistaxis have been reported in these investigations in the Service of Head Surgery at Camp Dodge Base Hospital. Of these individual records I have personally observed sixty cases, have made a detailed report of same and have endeavored to tabulate them for statistical and definite conclusions. These conclusions are:

1. This type of epistaxis occurred as a prodrome or as one of the earliest symptoms in the course of the "flu" epidemic.
2. The locality of the epistaxis seemed to be invariably on the septal side of the nose and in the course of the septal artery.
3. Bacteriologic findings indicate that the streptococcus hemolyticus was definitely identified as the causative factor in this form of epistaxis.
4. The cases in which the epistaxis occurred seemed to be those in which the most intense activity and more serious complications developed.
5. Where this epistaxis was spontaneous and violent, subsequent hemorrhage appeared in other localities of the respiratory tract or in other organs of the body.
6. Where epistaxis was found pneumonic complications were quickly presented.
7. Where epistaxis was not controlled by the sero-logical therapy that we carried out the end result to the patient in the large majority of cases was fatal.

In 1913 I conducted a series of observations* on the coagulation time of the blood in patients who presented themselves for operative work in the nose and throat, including the resection of the septum, adenoids, and tonsillectomy. At that time the reduction of coagulation-time of the blood by the use of normal sterile horse-serum was being investigated. In my series of cases I timed in each case the coagulation of the blood preceding the operation, injected 10 cc. of normal sterile horse-serum and again timed the blood coagulation prior to operation. I found that in every instance, even in those of hemophiliacs, the coagulation time, following the administration of the serum was reduced from one to three minutes and found that all patients that registered below the fixed coagulation time limit showed no tendency to hemorrhage during, or after, operation.

It occurred to me, therefore, that this type of epistaxis, associated with a specific micro-organism known to develop an

*Use of Normal Horse Serum as a Means of Controlling Hemorrhage in Oto-Laryngology. *The Laryngoscope*, October, 1913.

active hemolysis, might be materially benefited by the same form of serological therapy.

By co-operation with the department of general medicine and with the laboratories a general order was issued to inject 10 cc. of normal sterile horse-serum in all patients during the active "Flu" epidemic as soon as epistaxis was observed.

In sixty cases of epistaxis in which this serum treatment was promptly carried out, no mortality is recorded. These patients have been followed to final disposition, namely, to the pneumonia ward, to quarters, or to duty. Even where severe pneumonia developed, the patients have recovered.

It is a significant fact that in twenty-two cases in which epistaxis was found, but where the patient became violently ill and was transferred to the pneumonia wards before the serum could be injected, fifteen were fatal, developing pneumonia, empyema, other complications, and death. There is, therefore, a peculiarly significant relationship in the application of this serum therapy to the hemorrhage pathology developed in the course of this serious "Flu" epidemic. Hemorrhage seems to have been the key-note in the pathological status of each patient.

Another observation to corroborate this hemorrhagic intensity is found in a series of over seventy cases of so-called myringitis hemorrhagica. In these cases the membrana tympani presented either single or multiple, circumscribed, dark-red blebs which, on puncture, exuded a drop or two of bloody serum. In eight of these cases, the bacteriological culture of the contents of these belbs showed the presence of streptococcus hemolyticus. The clinical picture presented in this form of myringitis was not that of the usual acute myringitis where the membrana tympani is diffusely and uniformly congested, and where the mucosa of the tympanic cavity is less injected. The puncture of these blebs was limited to the external epithelial layer of the membrana tympani. and did not penetrate the tympanic cavity. Many of these cases, as far as the otologic conditions were concerned, cleared up without further invasion or treatment. Many were complicated by pneumonia and empyema. I merely wish to point to the corroborative evidence in this selective type of myringitis to a hemorrhagic condition closely associated with that found in the nasal and other respiratory mucous tracts.

The fauces, pharynx and the tonsils in almost all of the cases during the serious "Flu" period exhibited the same mahogany-red, intensely injected mucous membrane and swabs from these throats demonstrated the presence of streptococcus hemolyticus

almost without exception. These bacteriological findings run up into hundreds of cases, and when multiplied by similar observations made in the military hospitals throughout the country, into thousands of cases.

Within twenty-four to thirty-six hours after the initial symptoms were developed, in some instances shortly following epistaxis, in others where epistaxis did not occur, the case records of many patients show the admixture of pure blood with the sputum. This I take to be an indication of localized tracheal bleeding. Here again we have evidence of the same hemolytic changes in the mucous membrane of the trachea, or larger bronchi, followed by active bleeding.

In the report furnished by the medical officers in charge of the woman's wards where nurses and civilian females were cared for during the epidemic there is an interesting factor which further corroborates our hemorrhagic pathology, namely, in all epidemic "Flu" cases, menstrual hemorrhage occurred almost as early in the symptoms-complex as epistaxis, irrespective of the normal menstrual period of each patient. There were fewer cases of epistaxis among female patients than in male, but this may be accounted for by the fact that practically every female patient developed irregular menstrual hemorrhage.

In the post-mortem room we have not ceased to wonder at the enormous hemorrhagic character exhibited in the lungs and plural cavity in this epidemic. As someone significantly remarked—"These poor fellows seem to have been drowned in their own blood."

From the Genito-Urinary Department I received the report of several cases of intense hematuria. An autopsy of one patient revealed an active hemorrhage in the suprarenal capsule. In another autopsy the bladder was filled with blood and the mucosa of the bladder showed the same, diffusely injected, dark-red appearance as in the other mucosa tracts attacked by hemolytic changes.

It seems fairly logical, therefore, to conclude that hemorrhage in its various manifestations, hemolysis in its peculiar influence on the character of the mucous membrane and the streptococcus hemolyticus, in its frequent presence in so large a proportion of cases, must have some close pathological relationship and identity. There is still much discussion as to what was actually the original potent bacteriological cause of this epidemic. An eminent authority in bacteriology, terms the causative factor—"streptococcus hemolyticus plus," and the observa-

No.	REGISTER			SYMPTOMS (AT ONSET)										EPISTAXIS															General Observations	Bacteriological Findings	Final Disposition				Duration of Illness		
	Name	Occupation	Race	Temperature	Pulse	Chill	Cough	Coryza	Headache	Nausea	Conjunctivitis	Sore Throat	Backache	Previous Epistaxis	Bleeder	Injury to face	Diphtheria	Exanthemata	Typhoid	Previous Serology	Amount			Character of Coagulation			Location					Pneumonia Ward	Convalescent Ward	Quarters	Duty		
																					Slight	Moderate	Profuse	Recurrence	Prompt	Fair	Slow	Septum	Turbinate	Nasal Floor							
1	J.L.	R. R.	W.	100.6	90	*		*				*	*									*		1	*	*	*			Mild flu.			*			3 da.	
2	J.H.	Clerk	W.	100.	86							*	*					*				*		1	*	*	*			Otitis hemorrh.; flu				*		5 da.	
3	E.B.	Farmer	W.	102.2	88	*	*		*			*	*					*				*		1	*	*	*			Developed pneumonia		*		*		3 wks.	
4	H.G.	Nurse	W.	102.	126	*	*		*			*	*					*				*		2	*	*	*			Developed br. pneum.		*		*		4 wks.	
5	M.L.	Farmer	W.	103.4	112	*	*		*			*	*				*	*	*	*		*		2	*	*	*			Developed br. pneum.		*		*		3 wks.	
6	H.B.	Farmer	W.	100.4	86													*	*	*		*		3	*	*	*			Mild flu.		*		*		5 da.	
7	F.H.	Clerk	W.	102.2	130		*		*			*	*							*		*		1	*	*	*			Mild flu.			*		*	3 da.	
8	J.D.	Farmer	I.	104.4	110	*	*		*			*	*									*		1	*	*	*			Severe flu.		*		*		5 da.	
9	W.S.	Plumber	W.	103.8	104	*	*		*			*	*									*		1	*	*	*			Developed lob. pneum.		*		*		3 wks.	
10	W.K.	Butcher	W.	101.	84				*			*	*					*				*		2	*	*	*	*		Developed br. pneum.		*		*		2 wks.	
11	C.J.	Farmer	W.	103.4	98	*	*	*	*	*	*	*	*					*				*		2	*	*	*			Developed lob. pneum.		*		*		3 wks.	
12	R.W.	Farmer	W.	102.6	80	*	*		*	*	*	*	*					*				*		1	*	*	*			Developed lob. pneum.		*		*		3 wks.	
13	R.B.	Farmer	W.	100.	68	*	*		*			*	*			*		*				*		1	*	*	*			Developed lob. pneum.		*		*		3 wks.	
14	E.D.	Laborer	W.	101.6	88	*	*		*			*	*					*	*	*		*		1	*	*	*			Developed lob. pneum.		*		*		4 wks.	
15	S.V.	Laborer	N.	101.6	90				*			*	*					*	*	*		*		2	*	*	*			Severe flu.				*		2 wks.	
16	J.M.	Farmer	W.	101.2	100			*	*			*	*					*		*		*		5	*	*	*			Daily epistaxis.; flu				*		18 da.	
17	H.P.	Farmer	W.	103.4	90	*	*		*	*	*	*	*					*		*		*		1	*	*	*			Lob. pneumonia				*		27 da.	
18	H.S.	Farmer	W.	102.	94			*	*	*	*	*	*				*	*	*	*		*		2	*	*	*			Lob. pneumonia				*		3 wks.	
19	J.M.	Miner	W.	103.8	132		*	*	*	*	*	*	*					*		*		*		3	*	*	*			Mild flu.			*		*	12 da.	
20	J.P.	Machinist	W.	102.4	108		*	*	*	*	*	*	*				*	*	*	*		*		2	*	*	*			Mild flu.	Hem. strep. found.			*		6 da.	
21	W.W.	Laborer	N.	104.	118		*	*	*	*	*	*	*					*		*		*		4	*	*	*			Mild flu.			*		*	10 da.	
22	H.N.	Farmer	W.	100.8	82		*	*	*	*	*	*	*					*		*		*		5	*	*	*			Severe flu.	Hem. strep. found.			*		2 wks.	
23	B.C.	Laborer	N.	104.	95	*	*		*			*	*					*		*		*		5	*	*	*			Mild flu.			*		*	12 da.	
24	F.G.	Farmer	W.	104.6	112	*	*		*	*	*	*	*			*	*	*	*	*		*		8	*	*	*		Both sides	Severe flu.			*		*	6 da.	
25	S.B.	Farmer	W.	101.8	94	*	*	*	*	*	*	*	*				*	*	*	*		*		8	*	*	*		Both sides	Mild flu.			*		*	8 da.	
26	C.O.	Baker	W.	102.2	96	*	*	*	*	*	*	*	*					*		*		*		8	*	*	*		Both sides	Severe flu.	Hem. strep. found.			*		14 da.	
27	J.W.	Clerk	W.	102.6	84	*	*	*	*	*	*	*	*					*		*		*		8	*	*	*		Both sides	Mod. flu.			*		*	8 da.	
28	W.B.	Farmer	W.	100.2	80	*	*	*	*	*	*	*	*					*		*		*		6	*	*	*			Mod. flu.			*		*	13 da.	
29	O.W.	Farmer	W.	103.6	90			*	*	*	*	*	*					*		*		*		6	*	*	*			Mild flu.			*		*	5 da.	
30	W.B.	Laborer	W.	102.	92	*		*	*	*	*	*	*				*	*	*	*		*		6	*	*	*			Severe flu.			*		*	13 da.	
31	J.M.	Laborer	N.	103.	96	*		*	*	*	*	*	*					*		*		*		3	*	*	*			Mod. flu.			*		*	6 da.	
32	N.J.	Laborer	N.	101.2	96			*	*	*	*	*	*					*		*		*		3	*	*	*	Both sides		Mild flu.			*		*	8 da.	
33	A.R.	Farmer	W.	101.2	88				*			*	*					*		*		*		3	*	*	*			Mod. flu.			*		*	9 da.	
34	C.N.	Farmer	W.	102.4	96				*			*	*					*		*		*		3	*	*	*			Mild flu.			*		*	4 da.	
35	J.V.	Farmer	W.	102.2	106	*	*		*			*	*					*		*		*		3	*	*	*			Mod. flu.			*		*	6 da.	
36	C.T.	Teacher	W.	100.6	88			*	*	*	*	*	*					*		*		*		3	*	*	*			Mod. flu.			*		*	9 da.	
37	A.S.	Cashier	W.	102.6	92				*	*	*	*	*					*	*	*		*		3	*	*	*			Mild flu.			*		*	9 da.	
38	F.D.	Farmer	W.	101.4	92				*	*	*	*	*				*	*	*	*		*		3	*	*	*	Both sides		Mod. flu.			*		*	10 da.	
39	L.C.	Farmer	W.	102.	99	*	*		*			*	*					*		*		*		2	*	*	*			Mild flu.			*		*	6 da.	
40	J.M.	Farmer	W.	103.8	100		*	*	*	*	*	*	*					*		*		*		2	*	*	*			Mod. flu.			*		*	9 da.	
41	O.S.	Farmer	W.	101.4	96	*	*	*	*	*	*	*	*					*		*		*		3	*	*	*			Mild flu.			*		*	8 da.	
42	H.R.	Miner	W.	102.4	112			*	*	*	*	*	*					*		*		*		3	*	*	*			Mild flu.			*		*	10 da.	
43	O.M.	Carpenter	W.	103.	100	*			*	*	*	*	*					*		*		*		2	*	*	*			Mod. flu.	Hem. strep. found.			*		*	9 da.
44	H.H.	Clerk	W.	103.	108	*	*		*	*	*	*	*					*		*		*		2	*	*	*			Severe flu.			*		*	12 da.	
45	F.M.	Grocer	W.	100.2	96	*	*	*	*	*	*	*	*					*		*		*		2	*	*	*			Mod. flu.	Hem. strep. found.			*		*	15 da.
46	J.S.	Laborer	W.	103.2	120	*	*	*	*	*	*	*	*					*		*		*		2	*	*	*			Mild flu.			*		*	7 da.	

Black star in table used to indicate symptoms or conditions present.
Case No. 20—Nose broken during boxing some years ago.

Case No. 30—Nose broken from fall in childhood.
Case No. 37—Hookworm in 1912.

tions and conclusions that we might reach from the observations here reported are quite corroborative of this.

There have been many hypotheses and theories developed, but no tangible and absolute conclusions reached. The endothelial lining of the body is a protective mucosa. Hemolysis is created by the presence of the streptococcus hemolyticus. Wherever hemolysis in this mucous lining tract occurs there is a break in the continuity of these protective surfaces and a possible entrance for any form of aerobic micro-organism. These observations may throw but little light on the specific micro-organism or combination of micro-organisms that has actually made of this "Flu" epidemic one of the most violent forms of infection of the respiratory tract in this country, but it may offer some tangible evidence as to the character, course and form of invasion, by which such micro-organisms or combination of micro-organisms have attacked the lungs with such direful and destructive results.

In a survey of the accompanying detailed table a number of interesting features are in evidence. In cases numbered 19, 21, 25, 44, 46, 48, 49, 50, 51, 58, 59, and 60 streptococcus hemolyticus was found in the culture made from the blood taken during epistaxis. In Case 2 the same micro-organism was found in the hemorrhagic bleb from the ear.

With but few exceptions the nasal hemorrhage in each case ceased with normal promptness. In many the bleeding stopped spontaneously without any mechanical aids, but in cases numbered 3, 6, 8, 12, 14, 29, 34, 37, 40, 42, and 55 the nose was packed with gauze. In Cases 6, 8, 12, and 34 there was recurrence of epistaxis in from fifteen minutes to twenty-four hours notwithstanding the nasal pack. In Cases 4, 12, and 24 a second injection of ten cc. normal sterile horse serum was used.

It will be further noted that in all cases giving a history of previous epistaxis the hemorrhage during this influenza period was profuse.

In no instance had any of this selected series of sixty cases developed pneumonia at the time of their admission as far as could be clinically determined. All sixty cases showed the presence of streptococcus hemolyticus or of bacillus influenza, either in the blood culture from the nasal hemorrhage or from the swabs taken from the throat. Thirteen (13) of these cases developed pneumonia following influenza infection. Five of these thirteen cases showed the presence of pure blood mixed with

the expectoration coughed up from the deeper respiratory tract. This pure blood-mixed sputum was noted within twenty-four to thirty-six hours after the onset of symptoms and indicates, in my opinion, a process of hemolysis in the larynx, trachea or larger bronchi.

The severity of epistaxis does not seem to be an index of the severity of the infection, as many of these cases in which nasal hemorrhage was profuse developed mild types of influenza, and several of the cases in which epistaxis was moderate in amount developed serious and protracted pneumonia.

In conclusion let me emphasize these facts: (1) that each of these sixty cases was injected with ten cc. of horse serum as soon as the onset was reported; (2) that epistaxis occurred in each case as one of the symptoms of onset during the epidemic; (3) that bacteriological findings in each case corroborated the diagnosis of epidemic influenza; (4) that the entire series of sixty cases have been traced to their final disposition and that all have recovered.

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