

Described here the results of the efficacy of varied doses of gamma globulin used during an epidemic of infectious hepatitis in two Alaskan fishing villages.

EFFICACY OF VARIED DOSES OF GAMMA GLOBULIN DURING AN EPIDEMIC OF INFECTIOUS HEPATITIS, HOONAH, ALASKA, 1961

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IN RECENT YEARS much attention has been focused on finding minimal dose of gamma globulin effective in preventing clinical infectious hepatitis. Studies designed to determine the optimal dose have been primarily conducted in institutions for the mentally retarded, an environment in which susceptible individuals are often exposed to hepatitis over a period of months or years in contrast to the usual brief exposure that occurs in community outbreaks. Reported studies on the effect of gamma globulin in both urban and rural community epidemics have been retrospective in nature and have generally involved the evaluation of only one dose of gamma globulin. The study in this paper was undertaken to compare the relative efficacy of three different gamma globulin doses administered simultaneously during a widespread community epidemic. The three doses administered were 0.06 ml/lb, 0.01 ml/lb, and 0.005 ml/lb of body weight.

In August, 1961, members of the Communicable Disease Center, Arctic Health Research Center, and the Alaska Department of Health and Welfare participated in the investigation and control of an epidemic of infectious hepa-

titis in Alaska, involving two small Indian fishing villages, Hoonah and Excursion Inlet. Gamma globulin was administered to 619 individuals comprising 84 per cent of the susceptible population in the two villages at the height of the epidemic.

General

Hoonah is a small fishing village with a population in the winter of slightly over 800 persons. It is located on an island approximately 40 miles west of Juneau in southeast Alaska. The village consists almost entirely of Tlingit Indians, there being only some 20 non-native residents. Salmon fishing and crab canning comprise the basic industries of Hoonah.

Excursion Inlet is located 20 miles from Hoonah across a body of water called Icy Strait. It has a summer population of approximately 300 residents. About half of the Excursion Inlet inhabitants are members of Hoonah families who work from late June through September at the large salmon cannery there, frequently commuting back and forth between Hoonah and Excursion Inlet on weekends. When the

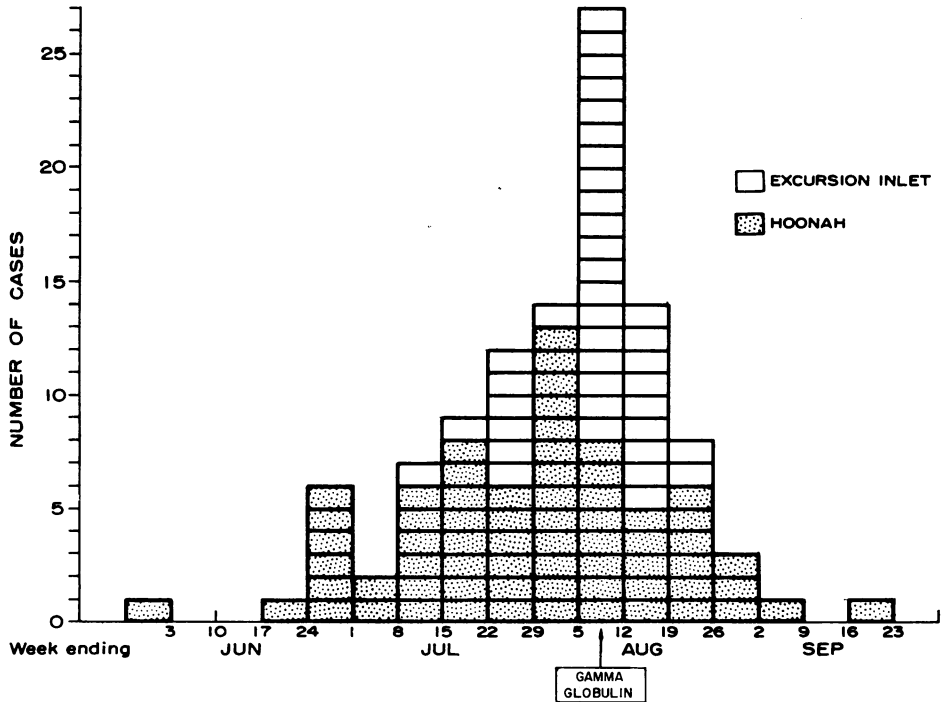


Figure 1—Hoonah-Excursion Inlet Infectious Hepatitis Epidemic, Cases by Week of Onset, 1961

cannery closes in September they return to their permanent homes in Hoonah.

In both villages the Indians live in crowded quarters consisting of two- to five-room frame houses generally within 50 feet of one another. All but a few homes have running water supplied from isolated reservoirs in each village. Both the community toilet in Excursion Inlet and individual flush toilets in most of the houses in Hoonah empty through the municipal sewage system into the bay, near the docks of each village. A 20-foot tide and 20 inches of rainfall each year help to prevent stagnation.

There is no history of a previous epidemic of hepatitis in either Hoonah or Excursion Inlet. Questioning of inhabitants revealed only eight cases of

hepatitis which occurred sporadically 11 to 41 years prior to the epidemic.

Method of Investigation

From August 5 to 16, 1961, a team of three physicians and a sanitary engineer participated in the investigation of the epidemic. It was assisted in the villages by a public health nurse who regularly spends alternate six-week periods in Hoonah; under normal circumstances there are no physicians in either Hoonah or Excursion Inlet.

During the first four days of the investigation the team visited all households with cases of hepatitis. Detailed case histories were taken and all individuals with recent illness were examined.

Gamma globulin was administered to

Table 1—Hoonah-Excursion Inlet, Alaska, Infectious Hepatitis Epidemic, 1961 Attack Rate by Age Group

Age Group	Total Population	No. of Cases	Attack Rate (%)
0-4	132	7	5.3
5-9	120	42	35.0
10-14	108	36	33.3
15-19	85	9	10.6
20-29	99	4	4.0
30-39	82	7	8.5
40-49	68	1	1.5
50+	120	0	—
Total	814	106	13.0

all presumed susceptibles who attended improvised clinics in Hoonah on August 9 and 10, and in Excursion Inlet on August 11 and 12. Two lots of gamma globulin supplied by the American Red Cross* were administered in a randomized fashion so that each person was as likely to receive 0.005 ml, 0.01 ml, or 0.06 ml gamma globulin per pound of body weight. At the time of administration complete household rosters were obtained including data on inoculated and uninoculated family members.

Follow-up surveillance was conducted by repeated visits to the villages by one or more of the team physicians during September and October and by the public health nurse who remained in the village for over five months after gamma globulin administration. Surveillance was also aided by a group of village women who regularly canvassed households for new cases. The list of nonimmunized individuals was supplemented by information gathered from a door-to-door survey during October, 1961.

A person was presumed to have had hepatitis if during the epidemic he experienced an acute illness characterized by one or more of the signs or symp-

toms in each of the "specific" and "non-specific" categories listed below.

"Specific":

- (1) history of brownish urine and/or whitish stools
- (2) right upper abdominal tenderness upon examination
- (3) hepatomegaly
- (4) bilirubinuria

"Nonspecific":

- (1) fever
- (2) anorexia
- (3) nausea, vomiting
- (4) upper abdominal pain
- (5) headache

A person was considered to have had icteric hepatitis if in addition he gave a history of jaundice or, upon examination, he was found to have either generalized jaundice or scleral icterus.

The Epidemic

The epidemic began in early June, 1961, when a child of a Hoonah family became ill approximately one month following a visit to another village. This index case infected children of several other families; the illness spread rapidly through the village. The virus was apparently taken into Excursion Inlet in late June by one of the first families infected and quickly spread through the Tlingit community there.

In all, 106 cases of infectious hepatitis occurred between June and September, 1961. The epidemic curve is shown in Figure 1. The time of gamma globulin administration is indicated as is the residence of the cases at the time of the epidemic. Of special note is the four-month duration of the epidemic and the sharp fall-off of cases shortly after gamma globulin administration.

Table 1 shows the attack rates by age groups for the epidemic. The over-all attack rate was 13 per cent. By far the greatest concentration of cases was in the 5-14-year-age group. Over 30 per cent of the children in these age groups developed infectious hepatitis.

* Squibb Laboratories—Lots: 330-2, 331-1.

Table 2—Hoonah-Excursion Inlet, Alaska, Infectious Hepatitis Epidemic, 1961

Number of Persons and Hepatitis Cases by Age Groups Receiving Each Dose of Gamma Globulin

Age Group	0.005 ml/lb Gamma Globulin		0.01 ml/lb Gamma Globulin		0.06 ml/lb Gamma Globulin		No Gamma Globulin	
	No. Received	Cases	No. Received	Cases	No. Received	Cases	No.	Cases
0-4	41	2	48	2	33	1	9	1
5-9	24	4	21	3	32	3	11	0
10-14	23	1	19	2	26	2	10	1
15-19	20	1	21	1	22	1	16	0
20-29	28	0	32	0	19	1	18	1
30-39	23	0	27	0	15	0	11	1
40-49	13	0	20	0	20	0	15	1
50+	23	0	29	0	40	0	28	0
Total	195	8	217	8	207	8	118	5

The cases were equally divided between the sexes.

Person-to-person transmission appeared to be the mode of spread in this epidemic. Virtually every case gave a history of contact with previous cases. The water supplies of each village came from isolated reservoirs and, in Hoonah, families using separate water supplies were also involved. Further, there were no large events or celebrations prior to the beginning of the epidemic at which a common exposure might have occurred. Lastly, the age-specific attack rates and the four-month duration of the epidemic are best explained by person-to-person transmission.

In general, the illness was mild with no fatalities. Less than 25 individuals, primarily adults, required hospitalization. There were no deaths. Of the 106 cases, 88 (83 per cent) were jaundiced; slightly more than 75 per cent had systemic complaints of fever, chills, anorexia, nausea, and vomiting.

Between August 9 and 12, at the peak of the epidemic, 619 individuals (representing 84 per cent of the population at risk) received gamma globulin. Of the 619 individuals immunized, 195 re-

ceived a dose of 0.005 ml/lb, 217 received 0.01 ml/lb, and 207 received 0.06 ml/lb (Table 2).

Results

Following the administration of gamma globulin, 29 individuals developed infectious hepatitis. As seen in Table 2, eight cases occurred in each of the three dosage groups; five occurred among those not inoculated. The cases that occurred after gamma globulin administration were again most frequently observed among children 5-14 years of age. Among the group not receiving gamma globulin the five postimmunization cases were generally older. It must, however, be noted that this group did not represent a control. It consisted of those individuals who did not appear at the clinics for gamma globulin; many were absent from the village during most or all of the epidemic.

The distribution in time of hepatitis cases with onset following gamma globulin administration is shown in Figure 2. There was a definite clustering of cases during the first week after gamma globulin administration among each of

the immunized groups. Although the number of cases is too small for firm conclusions, it is interesting to note that cases, both icteric and anicteric, occurred with approximately equal frequency among each of the dosage groups. Attack rates based on cases occurring more than six days after globulin administration (Table 3) reveal little difference between the test groups; those not given gamma globulin had a higher rate.

Discussion

In the initial studies¹ of gamma globulin efficacy in the prevention of clinical hepatitis, a dose of 0.15 ml per pound was used and found to be effective. The effectiveness of lower dosages, 0.06 and 0.12 ml/lb, among military

personnel² and among children in an orphanage³ was soon demonstrated. Later, an even smaller amount of gamma globulin, 0.01 ml per pound, was evaluated in a series of studies conducted during institutional outbreaks.⁴⁻⁶ This dosage similarly conferred good protection. Among household contacts during community outbreaks, Hsia, et al.,⁷ in 1954 observed only one case of hepatitis among 95 exposed individuals receiving 0.01 ml/lb as compared with 13 cases among 95 uninoculated individuals. Similarly, Ashley⁸ in 1954 found that 1.1 per cent of 269 exposed household contacts receiving 0.01 ml/lb developed hepatitis, while 16.8 per cent of 690 uninoculated household contacts became ill. Others,^{9,10} have also confirmed these findings.

Recent observations by Ward and

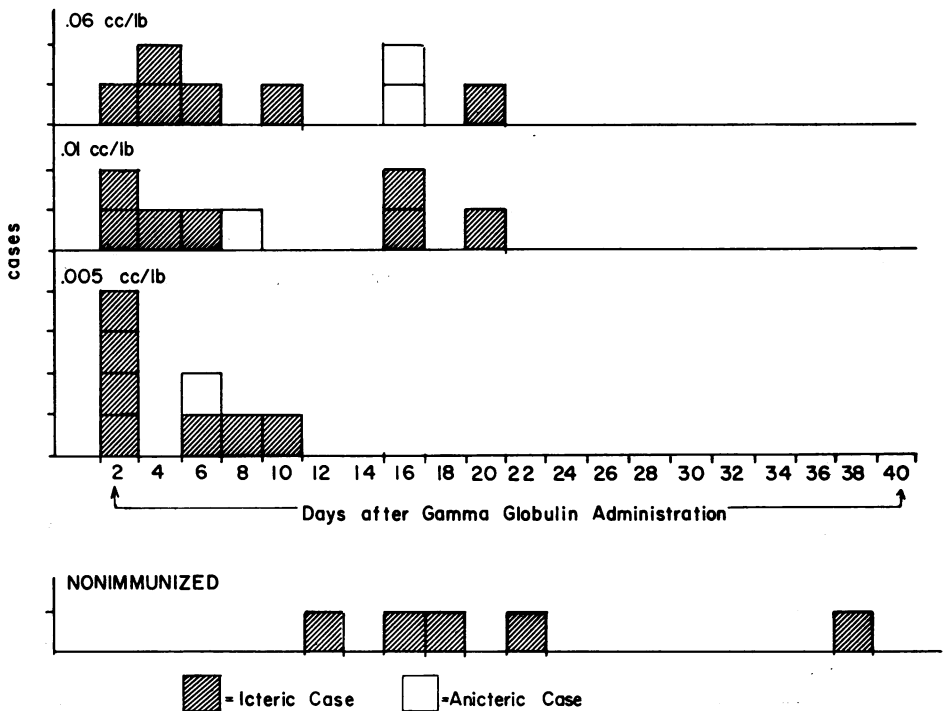


Figure 2—Onset of Infectious Hepatitis Cases by Two-Day Interval After Administration of Gamma Globulin, Hoonah-Excursion Inlet, Alaska, 1961

**Table 3—Hoonah-Excursion Inlet, Alaska
Infectious Hepatitis Epidemic, 1961**

Hepatitis Cases with Onset More Than Six Days
After Administration of Gamma Globulin

Dose of Gamma Globulin Administered	Population at Risk	Cases After Six Days	Per cent
0.005	195	2	1.0
0.01	217	4	1.8
0.06	207	4	1.9
Total	619	10	1.6
No gamma globulin	118	5	4.2

Krugman,¹¹⁻¹³ based on studies conducted in an institution where hepatitis is endemic have questioned the adequacy of the dosage of 0.01 ml/lb. This dosage in their first trial did not appear to produce the high degree of protection for either the inmates or the employees of the institution as compared to the protection afforded by 0.06 ml/lb of body weight in later trials.

The study reported was undertaken to provide some additional data on the question of gamma globulin dosage. At the time of globulin administration the virus was widespread in the two communities; gamma globulin had not been administered in the villages. Previous outbreaks in Alaskan Indian villages¹⁴ suggested that the epidemic might well persist for as long as eight months with over-all attack rates of 28 per cent or more. However, following gamma globulin administration, the epidemic in Hoonah subsided surprisingly rapidly and after 38 days no cases were observed over the succeeding six months.

Although 24 cases occurred among the three study groups, most occurred during the immediately succeeding week; only ten occurred after the sixth day. The equal distribution of cases both in severity and time suggests there

was no effective difference in protection based on dosage.

Additional cooperative studies employing different dosages of gamma globulin from a single lot are in progress.

Summary

A total of 106 cases of infectious hepatitis occurred among 814 individuals in Hoonah and Excursion Inlet, Alaska, from June through September, 1961. At the height of the epidemic gamma globulin was administered in random fashion to 619 or 84 per cent of the population at risk in dosages of 0.005 ml/lb, 0.01 ml/lb, and 0.06 ml/lb of body weight. Shortly following administration of gamma globulin there was an abrupt fall-off in the number of cases of clinical hepatitis. Although a true control group was lacking, the sharp drop-off in the epidemic curve following gamma globulin administration and the clustering of post gamma globulin cases during the first week after inoculation suggests that gamma globulin was effective in terminating the epidemic. If gamma globulin administration was effective in the two Indian villages, this study would indicate that there was no significant difference in this epidemic in the relative efficacy of 0.005 ml/lb, 0.01 ml/lb, and 0.06 ml/lb of body weight.

ACKNOWLEDGMENTS — The authors of this paper would like to express their sincere appreciation of the many members of the Alaskan Department of Health and Welfare, Arctic Health Research Center, and Communicable Disease Center, whose combined efforts made this study possible. In particular, we would like to cite the assistance of Dr. Larry Winter and Dr. James Maynard during the investigation; Dr. James Mosley and Dr. Alexander Langmuir for their critical review and analysis of the study and paper; and Dr. James Pert and Dr. Sam Gibson of the American Red Cross for supplying the gamma globulin for this and subsequent cooperative studies.

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This paper was presented before a Joint Session of the Epidemiology and Health Officers Sections of the American Public Health Association at the Ninetieth Annual Meeting in Miami Beach, Fla., October 16, 1962.

This study was conducted by members of the Epidemiology Branch, Communicable Disease Center, USPHS, Arctic Research Health Center, USPHS, and Alaskan Department of Health and Welfare.

Memorial Fund Honors Alfred L. Burgdorf

A memorial fund is being established in honor of Dr. Burgdorf, for 22 years health director of the Hartford (Conn.) Health Department, who died in 1962. It is proposed that the memorial include the renaming of the Hartford Health Department to the Dr. Alfred L. Burgdorf Health Center, an annual lecture in public health and preventive medicine, and the creation of a permanent public health library fund. Those wishing to contribute should make checks payable to the Alfred L. Burgdorf, M.D., Memorial Fund, to be forwarded to the Hartford National Bank and Trust Company.