A Preliminary Report on Effects of Routine Military Inoculations on Respiratory Illness.* (28680)

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(Introduced by Thomas G. Ward)
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Acute respiratory illness of military recruits typically peaks in early weeks of the basic training period(1); one of the potentially important factors operative at this time is the treatment of all men with the bulk of the routine inoculations. Since inoculation reactions may aggravate a pre-existing minor illness, it is certainly possible that the large number of routine inoculations may be contributory to the etiology of the more severe respiratory illnesses that make the military recruit so different from "seasoned" personnel or his civilian counterparts.

Materials and methods. The study of this problem, without interfering with the basic training of new men, was effected from January 1 to April 24, 1961, by placing part of the arriving new men coming to Great Lakes Naval Training Center on a delayed inoculation schedule, for comparison to the others who were placed on the regular schedule. Table I shows the 2 schedules by weeks of training period. The new men were formed into training companies of about 66 men and processed for inoculations and other aspects of training as company units; hence, the 2 inoculation schedules could not easily have been evaluated simultaneously in men of the same training company.

Results have been obtained for about 5,000 men from 77 companies treated according to the regular schedule and about 4,300 men from 65 companies treated according to the delayed inoculation schedule. (Data for about 45,000 men for all of 1961 will later become available.) Both regular and delayed companies were formed during each week of the study, but not always in equal numbers. Knowledge of the schedule differences could not be concealed from the recruits, nor could placebos have been humanely given on a matched basis; a number of checks indicated that the recruits or the instructors had little concern for the schedule differences. For the most part these differences were accepted as some kind of poorly understood administrative procedure.

Respiratory illness data are based on men voluntarily reporting to sick call, the details and definitions of which are the same as previously employed(1). Pneumonia diagnosis was made from X-rays read without knowledge of the patient's inoculation status.

Results. Table II shows that significantly less of the severe respiratory illnesses were reported during the first period of training by

TABLE I. Inoculation Schedule.

Time given	Regular	Delayed
Processing	Polio Adenovirus Influenza	Polio Adenovirus Influenza
1st week	Smallpox Tetanus & diphtheria Typhoid	
2nd "	Typhoid Benzathine penicillin	Benzathine penicillin
3rd "	Typhoid	
4th "		
5th "	Tuberculin test Tetanus & diphtheria Polio	Tuberculin test Tetanus & diphtheria Smallpox Typhoid
6th "		"
7th "		"
8th "		
9th "		Tetanus & diphtheria Polio

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TABLE II. Numbers of Cases and Illness Rates/1000/Week Reported by Men Inoculated According to the Regular and Delayed Schedule, 1961, Great Lakes, Ill.

Clinical category		1st period of training			2nd period of training		
		Schedule		Statistical	Schedule		Statistical
		Regular	Delayed	significance*	Regular	Delayed	significance*
Resp. ill. hosp.							
Pneumonia	No.	113	83	$F_{(168, 226)} = 1.15$	53	30	$F_{(62, 106)} = 1.46$
	Rate	5.6	4.8	$P = .165$	2.1	1.4	$P = .043$
Other	No.	1488	928	$F_{(1858, 2976)} = 1.37$	534	462	$F_{(1070, 924)} = 1.01$
	Rate	73.5	53.7	$P < .0001$	21.1	21.4	$P = .432$
Resp. ill. outpatients							
Febrile	No.	239	182	$F_{(386, 478)} = 1.12$	40	37	$F_{(82, 74)} = 1.06$
	Rate	11.8	10.5	$P = .132$	1.6	1.7	$P = .406$
Afebrile	No.	569	386	$F_{(774, 1138)} = 1.26$	144	117	$F_{(236, 288)} = 1.04$
	Rate	28.1	22.3	$P = .240$	5.7	5.4	$P = .368$
Non-resp.							
Rubella	No.	293	258	$F_{(588, 516)} = 1.03$	83	69	$F_{(140, 166)} = 1.01$
	Rate	14.5	14.9	$P = .376$	3.3	3.2	$P = .467$
Other	No.	255	180	$F_{(362, 510)} = 1.20$	299	261	$F_{(600, 522)} = 1.02$
	Rate	12.6	10.4	$P = .027$	11.8	12.1	$P = .415$
Severe resp. ill.	No.	1840	1193	$F_{(2388, 3680)} = 1.32$	627	529	$F_{(1060, 1254)} = 1.01$
(feb. & hosp.)	Rate	90.0	69.0	$P = .018$	24.8	24.5	$P = .480$
All episodes	No.	2959	2014	$F_{(4080, 5918)} = 1.25$	1154	977	$F_{(1956, 2308)} = 1.01$
	Rate	146.2	116.5	$P = .008$	45.6	45.2	$P = .498$
No. men		5060	4322		5060	4322	

* Test based on Poisson distribution, along lines of Fisher's exact test for the binomial distribution. Probabilities were approximated by evaluating the normalized F values, with the indicated degrees of freedom, on a high speed digital computer.

men from the delayed schedule companies. Fig. 1 indicates that this effect on all febrile and/or hospitalized respiratory illness cases did not accrue in any one period nor did not result from the unequal allotment of companies to the 2 schedules at differing periods of risk. Even with the variability in the weekly rates, the effect of the schedule differences appears to have been operative during the entire period. In Fig. 2 the same data are shown according to the week of training in which the illnesses were reported. The schedule effect appears in the first week and becomes maximal by the second week of training. While on a smaller scale, this was substantiated in the fifth and sixth weeks where the delayed companies (then receiving the bulk of the inoculations) reported relatively more illness.

Data for pneumonias show similarly reduced rates in men from the delayed schedule (the differences, in the first period, are not statistically significant, $P = .165$, but significantly less pneumonia occurred in the delayed companies during the second period). It is interesting to note that non-respiratory illness also followed the same patterns, but with smaller relative differences. Rubella cases showed a delay of about one week in association with the delayed schedule. Non-respiratory conditions other than rubella include cases diagnosed as inoculation reactions and other non-definitive cases (headaches, malaise, etc.) which cannot be classified as respiratory illness, but could be affected by inoculation reactions. Thus, fewer inoculation reactions and their effects on other non-respiratory conditions appear to account for the pattern and the approximate 6% reduction in incidence associated with the delayed inoculation schedule.

Discussion. The routine military inoculations seem to be associated with about a 20% greater incidence in severe respiratory ill-

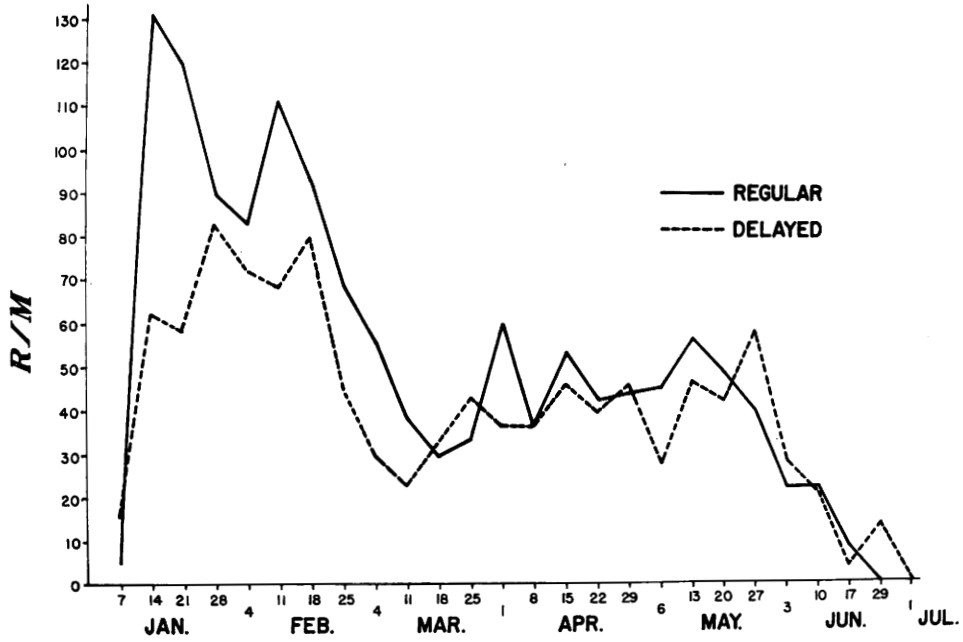

FIG. 1. Febrile and/or hospitalized respiratory illness rates reported by recruits in the delayed and regular schedule companies, Great Lakes, Ill.

nesses. Peak rates of illness were 35 to 25% less in the second and third weeks of training, in association with the delayed inoculation schedule. However, the general pattern of respiratory illness by weeks of training remained essentially unchanged. Since the relative differences in rates between the 2 schedules are comparable in magnitude to the effects of what have been considered highly effective vaccine(1), used in respiratory illness prophylaxis, this indicates a potentially important area for further study, *i.e.* the non-specific and non-infectious factors in the etiology of recruit respiratory illness.

Summary. Preliminary results are reported from a study of the non-specific effects of routine military inoculations on respiratory illness reported by navy recruits, Great Lakes, Ill. Delaying most of the inoculations to the latter half of the basic training period was associated with about a 20% reduction in the incidence of the more severe respiratory illnesses, including pneumonia. The general pattern of respiratory illness was unaltered by delaying the inoculations; hence, possibly other non-infectious factors also contribute to the etiology of recruit respiratory illness.

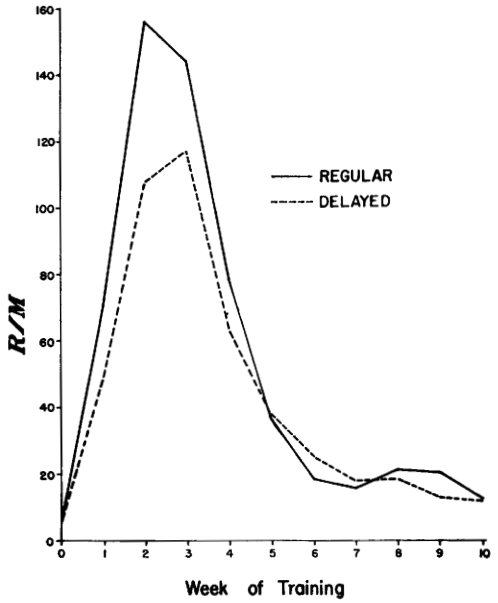

FIG. 2. Febrile and/or hospitalized respiratory illness rates reported by recruits in each week of training in delayed and regular schedule companies, Great Lakes, Ill.

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Studies on the Structure of Mouse Antibodies.* (28681)

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Mammalian 7S gamma globulins have been shown to be made of two types of polypeptide chains which can be separated by reduction in 8M urea and starch gel electrophoresis in 8M urea(1). They have been called Light (L) and Heavy (H) chains(2). In human immune globulins, the H chains characterize the different antibody types γ_2, γ_{1A}, γ_{1M}(2). The heterogeneity of γ-globulins within a given type appears to depend in part on the heterogeneity of the L chains. Normal human or guinea pig 7S γ-globulin, upon reduction and alkylation and electrophoresis in 8M urea starch gel, yield patterns showing a strong slow band corresponding to the H chains and a faster moving smear corresponding to the L chain components(1,3). In contrast, human myeloma(4) and purified guinea pig anti-hapten antibodies from individual animals(3), similarly treated, show distinctive sharp bands with well-defined mobility corresponding to L chains. Furthermore, in the case of guinea pig antibodies the number and mobility of the bands yielded by antibodies against non-cross-reacting haptens seem to be characteristic of the immunological specificity(5).

Guinea pig 7S antibodies against a single specificity have also been found to consist of 2 families of antibodies γ_1 and γ_2 with different electrophoretic mobility(6). These antibodies have been shown to mediate different biological activities in the guinea pig; γ_1 antibodies being responsible for anaphylactic sensitivity(7) and γ_2 antibodies for such phenomena which depend upon the fixation of hemolytic complement such as cell lysis and the Arthus reaction(8). γ_1 and γ_2 guinea pig antibodies share common antigenic determinants of their S fragments (Piece I and II of Porter) and possess distinct antigenic determinants of their F fragments (Piece III of Porter)(9).

The present study attempts to characterize the antibodies which are produced by individual mice hyperimmunized against well-defined haptens or foreign proteins, as was done for the guinea pig.

Purified antibodies from individual mice appear also to contain at least 2 families of molecules, with slightly different electrophoretic mobility, possessing similar as well as distinct antigenic determinants. Purified anti-hapten antibodies from single mice, when reduced and alkylated and subjected to electrophoresis in 8M urea, yielded distinct bands corresponding to L chains, while mouse γ-globulin or purified anti-ovalbumin antibodies similarly treated showed a smear corresponding to the zone of L chain migration.

Methods. Animals. Random bred Swiss Webster and pure strain C_3H mice were used.

Antigens. Ovalbumin 2 $\times$ recrystallized, Worthington Biochemical Corp.

Beef γ-globulin, Armour, Chicago, Ill.

2,4-dinitrophenyl bovine γ-globulin (DNP-BGG). Prep. I; 8 groups/mole, prep. II; 45 groups/mole.

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