the courts, in reaching their decisions, were not influenced at all by evidence of urine-alcohol concentrations. Clearly, however, this conclusion can only be tentative at this stage. To test it more strictly, more account would have to be taken of other factors influencing the decisions; to do this it would be necessary to consider a much larger number of cases.

Finally, attempts were made by constructing 2 by 2 contingency tables to find whether there was any relationship between the occurrence of accidents on the one hand and the plea of the defendant or the decision of the court on the other. Again only cases medically pronounced unfit to drive were considered. There appeared to be no significant relationship whatever. That is, whether or not an accident had occurred appeared to have no bearing on the probability of the defendant pleading guilty, or on the decision of the court if he pleaded not guilty.

All of the cases considered here came from south-west England. It would be interesting to see a similar analysis for a comparable or, preferably, larger series of cases from the whole country, or at least from other regions of it.

Summary and Conclusions

The urine-alcohol concentrations of persons arrested for driving whilst under the influence of drink appear to be normally distributed around a mean value of 300 mg./100 ml.

The mean figure for cases in which accidents occurred is significantly lower than that for cases in which the defendants were driving without accident.

The probability of the defendant being medically pronounced unfit to drive rises with increasing urine-alcohol concentration up to a figure of about 220 mg./100 ml., but above this figure appears to be about the same for all concentrations.

The statistical evidence available suggests that the decisions of the courts are not influenced at all by legal evidence of urine-alcohol concentrations.

The statistical evidence available also suggests that there is no relationship between the incidence of accidents and the pleas of the defendants or decisions of the courts.

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Nursing for Men is a new title in the "Choice of Careers" booklets issued by the Central Youth Employment Executive. It describes nursing for men in and outside hospitals, training, conditions of service, and openings and prospects. Mental and mental deficiency nursing were the first branch of the profession in which men could qualify, and these still offer the best opportunities for the male nurse, states the booklet. The first male nurse was accepted for general training in 1930, and now there are many hospitals where they can receive training. This booklet is prepared by the Ministry of Labour and National Service and the Central Office of Information. It is obtainable from H.M.S.O., price 1s. 6d. net.

EXPERIMENTAL INVESTIGATION OF THE RELATIONSHIP BETWEEN METHOD OF TREATMENT AND SUBSEQUENT IMMUNITY*

BY

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Although children with acute respiratory infection respond well to a single large dose of penicillin or sulphonamide (Platt, 1940; Lauria, 1947; Wilken-Jensen, 1948; Friderichsen and Walther, 1950; Jersild *et al.*, 1956; Joseph, 1958), it is not known whether the immunity following this method of treatment differs from that following repeated chemotherapy. This treatment with a single large dose has been called stoss therapy by Gaisford (1951), a name originally given by Harnapp (1938) to a method of treatment of rickets with a single massive oral dose of vitamin D.

Good immunity in rabbits and mice developed following sulphapyridine treatment of pneumococcal infection (Whitby, 1938a; Larson *et al.*, 1939; Curnen and MacLeod, 1942). This immunity was the same in quantity, quality, and speed of production as that created by orthodox active immunization (Whitby, 1938b), and the degree of immunity was related quantitatively to the size of the infecting dose (McIntosh and Whitby, 1939).

The action of penicillin, however, differs from that of sulphonamide, and immunity following treatment with penicillin may be different. McIntosh and Whitby (1939) showed that sulphapyridine exerted its bacteriostatic action only after a lag of several hours, thus allowing time for the formation of antibody, whereas MacLeod and Stone (1945) have pointed out that by contrast the action of penicillin was immediate and might be independent of an immune response. Thus Harrison (1946) showed that, when penicillin was given to rabbits four hours after infection, no antibody response could be detected; when he reinfected his survivors all the animals previously saved by penicillin died in five to six days as compared with controls, which died in 36 hours. By contrast, rabbits saved by penicillin given 24 hours after infection, when reinfected, survived and showed a high titre of antibodies. Harrison (1946), with mice, and Skinsnes and Woolridge (1948), with protein-depleted rats, obtained similar results.

Present Investigation

White male mice of Parkes A strain were used. They were infected with a known dose of type I pneumococci (NCTC 7465), and divided into three groups: (1) single dose (stoss), (2) repeated doses, and (3) untreated. Ten days after the original infection, the survivors in groups 1 and 2, and a new control group, were each infected with a challenging dose of pneumococci, and the degree of immunity was measured by mortality.

My preliminary experiments showed that the optimum interval between infection and treatment was 10 hours, which agrees with the findings of Harrison (1946) and Skinsnes and Woolridge (1948). Too high a mortality resulted if the mice were left untreated for longer periods.

*Based on M.D. thesis for University of Cambridge, 1957.

Treatment.—Although studies of the combination of sulphamide and penicillin *in vitro* (Ungar, 1943; Rammelkamp and Keefer, 1943; Bigger, 1944b; Garrod, 1944; Kirby, 1944; Hobby and Dawson, 1944) or *in vivo* (Sultan *et al.*, 1945; Nitti *et al.*, 1946) have not shown clear-cut results, such a combination was used in these experiments in order to resemble common clinical practice. The dose of both penicillin and sulphadimidine was calculated on body weight, and was proportional to that usually given to a child. For 20-g. mice the single dose was 600 units of penicillin and 6 mg. of sulphadimidine, and the repeated dose was 100 units of penicillin and 1.3 mg. of sulphadimidine eight-hourly for six doses.

The size of the challenging dose also had to be gauged by preliminary experiment. The aim was to achieve a mortality of between 50% and 100% of controls, which allowed differences to appear between the groups of treated animals. In all experiments except one the challenging doses were of two strengths so as to facilitate distinction between the treated animals.

Methods

Seven experiments consisting of the primary infection and its treatment were performed, each using 150 mice (and on one occasion 180). There were 13 reinfection experiments, because with one exception the survivors from the primary infection were divided into two equal groups and reinfected with two different challenging doses. The experiments followed the same pattern, but the size of both the primary and the challenging infecting dose varied, so that the results were reasonably broad. The pneumococci were frequently passaged through mice, but an unusually large number of organisms had to be injected to produce the mortality needed.

On the day before the experiment an infected mouse was killed and heart blood was streaked on blood agar and incubated. Eighteen hours later a glucose-broth culture was prepared from the agar and was incubated for six hours. This broth was serially diluted, colony counts were made, and doses of 0.2 ml. were injected intraperitoneally in mice. The 150 infected mice were left untreated for 10 hours. Preliminary experiments had shown that blood cultures were positive at this time. Fifty mice were then given only one injection of a freshly prepared mixture of 600 units of sodium penicillin and 6 mg. of sodium sulphadimidine. A further 50 mice were injected with a mixture of 100 units of sodium penicillin and 1.3 mg. of sodium sulphadimidine, and this was repeated for six doses at eight-hourly intervals. The remaining 50 infected mice were left untreated.

The three groups of mice were observed for the next ten days, and the heart blood and peritoneal exudate of the treated animals that died were cultured. At the end of this period the survivors in each group, and a fresh group of 50 controls, were reinfected with pneumococci intraperitoneally, prepared as for the initial infection. The actual dose varied with the experiment. The animals were left untreated and the mortality and day of death noted; the heart blood and peritoneal exudate of those that died after the third day were cultured.

Colony counts were done by the method of Miles *et al.* (1938). Counting was made easier by staining with Janus green (Joseph and Mann, 1958) and using a graticule and binocular microscope.

Results: Primary Infection

Experiment 4 has been selected as representative and is described in detail. The differences found in the other experiments are pointed out below.

Experiment 4

Three groups (each of 50 mice) were injected intraperitoneally with 0.2 ml. of a 1 in 100 dilution of a six-hour glucose-broth culture of pneumococci (about 750,000 organisms). One animal in the stoss group died a few minutes

after the injection; post-mortem examination did not reveal the cause of death. This death has not been recorded as due to pneumococcal infection. Ten hours later about two-thirds of the animals looked ill, had ruffled coats, and were sluggish and unresponsive. Some of the others showed these signs to a lesser degree. At this time the 49 in the stoss group received an intramuscular injection of 600 units of sodium penicillin and 6 mg. of sodium sulphadimidine in 0.3 ml. of sterile water, and the 50 in the repeated group 100 units of sodium penicillin and 1.3 mg. of sodium sulphadimidine. Fifty animals were left untreated.

This first treatment was given at midnight; progress was next observed eight hours later, when the repeated group received a further injection. At this stage the change in the mice was remarkable; all in the stoss and most in the repeated groups were lively, alert, and had smooth coats, and only a few in the latter group were slightly ill. Eight hours later the mice in the repeated group were treated again, and both they and those in the stoss group now looked identical. The repeated group were treated six times altogether at eight-hour intervals. In this experiment, except for the one early chance death, all animals in the treated groups survived during the 10-day observation period, and on this day they looked fit and there was no outward indication that they had been infected. In the control group several mice died between 10 and 18 hours after infection, and by the end of 24 hours 14 (28%) had died (Table I). Neither the immediate death in the stoss group (already

TABLE I.—Experiment 4. Length of Survival. Primary Infection

Group	No. of Mice	Day of Death										Total Deaths
		1	2	3	4	5	6	7	8	9	10	
Stoss	49*											0
Repeated	50											0
Controls	50	14	13	7	1						1†	35 (70%)

* Broth diluted 100 times. Dose contains 750,000 organisms.

† One sudden death immediately after infection. No cause at necropsy.

‡ No pneumococci grown from heart blood or peritoneal exudate.

mentioned) nor the death of a control mouse on the tenth day has been ascribed to pneumococcal infection in view of the negative smears and culture for pneumococci. The final mortality in the control group was 35 (70%).

All Experiments

Table II summarizes the results of primary infection in each experiment. In experiments 3, 5, 6, and 7 a greater number of mice died in the stoss group than in the repeated

TABLE II.—All Experiments. Mortality. Primary Infection

Experiment	Group	Dose of Organisms	No. of Mice	No. Dying
1	Stoss	2,000	50	0
	Repeated	2,000	50	0
	Controls	2,000	50	17 (34%)
2	Stoss	150,000	50	0
	Repeated	150,000	50	0
	Controls	150,000	50	22 (44%)
3	Stoss	800,000	60	3 (5%)
	Repeated	800,000	60	0
	Controls	800,000	60	34 (57%)
4	Stoss	750,000	50	0
	Repeated	750,000	50	0
	Controls	750,000	50	35 (70%)
5	Stoss	690,000	50	5 (10%)
	Repeated	690,000	50	0
	Controls	690,000	50	50 (100%)
6	Stoss	830,000	50	2 (4%)
	Repeated	830,000	50	0
	Controls	830,000	50	50 (100%)
7	Stoss	830,000	50	14 (28%)
	Repeated	830,000	50	10 (20%)
	Controls	830,000	50	49 (98%)

group, but the difference was small and was never sufficient to interfere with the completion of the experiment. Thus a reasonable and comparable number of mice from each treatment group were available for reinfection.

Results : Reinfection

Experiment 4.—The results of reinfection in experiment 4 are shown in Table III. Two different reinfesting doses were used as in every other experiment except No. 1. It

TABLE III.—*Experiments 4a and 4b. Mortality and Length of Survival. Reinfection*

Group	No.	Day of Death										Total Deaths
		1	2	3	4	5	6	7	8	9	10	
<i>Broth diluted twice. Dose contains 16.5×10^6 organisms</i>												
Stoss	24	9	8									19 (79%)
Repeated	25	11	8	2	1							22 (88%)
Controls	25	8	7									25 (100%)
<i>Broth diluted 10 times. Dose contains 3.3×10^6 organisms</i>												
Stoss	25	3	6	2	0	1	1					13 (52%)
Repeated	25	4	11	3								18 (72%)
Controls	25	15	7	3								25 (100%)

was interesting that the difference in the size of the reinfesting dose was sufficient to reduce the mortality in the stoss group from 79% to 52%, and in the repeated group from 88% to 72%. The days on which the mice died are also shown.

Remaining Experiments

In all experiments except one the results differed in degree rather than pattern (Table IV).

TABLE IV.—*All Experiments. Results of Reinfection. Mortality*

Exp.	Group	Dose of Organisms	No. of Mice	Deaths	Percentage Mortality	Significance (P)*	Av. Survival Time (Days)
1a	Stoss	63×10^6	49	38	77	0.1-0.05	2.2
	Repeated	63×10^6	50	46	92		0.8
	Controls	63×10^6	50	50	100		0.2
2a	Stoss	3×10^6	25	13	52	0.2-0.1	5.8
	Repeated	3×10^6	25	19	76		3.2
	Controls	3×10^6	25	24	96		1.1
2b	Stoss	3×10^5	25	1	4	0.1-0.05	9.6
	Repeated	3×10^5	25	1	4		9.6
	Controls	3×10^5	25	19	76		3.3
3a	Stoss	6×10^5	27	13	48	0.1-0.05	5.8
	Repeated	6×10^5	29	6	21		8.1
	Controls	6×10^5	30	27	90		2
3b	Stoss	6×10^4	27	3	11	0.1-0.05	9.1
	Repeated	6×10^4	29	3	10		9.1
	Controls	6×10^4	30	18	60		4.6
4a	Stoss	16.5×10^6	24	19	79	0.3-0.2	2.6
	Repeated	16.5×10^6	25	22	88		1.9
	Controls	16.5×10^6	25	25	100		0.3
4b	Stoss	3.3×10^6	25	13	52	0.3-0.2	5.6
	Repeated	3.3×10^6	25	18	72		3.5
	Controls	3.3×10^6	25	25	100		0.5
5a	Stoss	31×10^4	21	6	29	0.01-0.001	7.3
	Repeated	31×10^4	25	18	72		3.4
	Controls	31×10^4	25	22	88		1.5
5b	Stoss	93×10^3	21	3	14	0.02-0.01	9.0
	Repeated	93×10^3	25	13	52		5.2
	Controls	93×10^3	25	18	72		0.9
6a	Stoss	167×10^2	24	3	12	0.2	9.2
	Repeated	167×10^2	25	8	32		7.2
	Controls	167×10^2	25	25	100		0.9
6b	Stoss	5×10^3	24	5	21	0.2	8.5
	Repeated	5×10^3	25	6	24		7.9
	Controls	5×10^3	25	25	100		1.2
7a	Stoss	167×10^2	18	0	0	0.01-0.005	10
	Repeated	167×10^2	20	1	5		9.6
	Controls	167×10^2	25	24	96		2.1
7b	Stoss	5×10^3	18	0	0	0.01-0.005	10
	Repeated	5×10^3	20	1	5		9.6
	Controls	5×10^3	25	22	88		3.3
Total	Stoss		328	116	35.7	0.01-0.005	
	Repeated		348	162	47.6		
	Controls		360	322	89.4		

* Chi-square with Yates correction.

The mortality on reinfection of the treated groups showed a wide variation. In the stoss group the mean mortality was 35.7% (range 0 to 79%), in the repeated group it was 47.6% (range 4 to 92%), and in the control group it was 89.4% (range 60 to 100%).

In experiments 5a and 5b the lower mortality in the stoss group was significant at the 1% level. In experiment 1a the difference was nearly significant at the 5% level in

TABLE V.—*All Experiments. Reinfection. Survival for 2 Days or Less Compared with Survival for more than 2 Days*

Exp.	Group	Total	Survived 2 Days or Less	Survived More than 2 Days	P*
1a	Stoss	49	38	11	0.1-0.05
	Repeated	50	46	4	
2a	Stoss	25	3	22	0.05-0.02
	Repeated	25	11	14	
2b	Stoss	25	1	24	0.3-0.2
	Repeated	25	0	25	
3a	Stoss	27	10	17	0.3-0.2
	Repeated	29	6	23	
3b	Stoss	27	2	25	0.2-0.1
	Repeated	29	3	26	
4a	Stoss	24	17	7	0.01-0.001
	Repeated	25	19	6	
4b	Stoss	25	9	16	0.2-0.1
	Repeated	25	15	10	
5a	Stoss	21	6	15	0.01-0.001
	Repeated	25	17	8	
5b	Stoss	21	2	19	0.02-0.01
	Repeated	25	12	13	
6a	Stoss	24	2	22	0.02-0.01
	Repeated	25	6	19	
6b	Stoss	24	3	21	0.02-0.01
	Repeated	25	4	21	
7a	Stoss	18	0	18	0.02-0.01
	Repeated	20	1	19	
7b	Stoss	18	0	18	0.02-0.01
	Repeated	20	0	20	

* Chi-square with Yates correction.

favour of the stoss group, and in experiment 3a at the same level in favour of the repeated group. In the remaining nine experiments any difference found might have been due to chance. However, in four of these the small differences which occurred were in favour of the stoss group; in the remaining five experiments the results were almost identical in the two groups.

Mortality within**Two Days.**

The number not surviving the first two days was compared with the number surviving more than two days (Table V). In experiments 5a and 5b the differences were great, and highly significant; in experiment 2a the difference was significant at less than 5%, and in experiment 1a almost at the 5% level. In the remaining experiments the differences were small.

Total Results.—The individual results of each experiment have been added together and are shown in Table IV. The mortality in the stoss group was 35.7% and in the repeated group 47.6%. The probability of this difference occurring by chance was less than 0.01. The cumulative percentage mortality is shown in the Chart.

Discussion**Reinfection**

The results of reinfection are discussed first, since they form the main purpose of the investigation.

In general, fewer or the same number of mice died in the stoss group compared with the repeated group; the similar

Cumulative percentage mortality on reinfection. Difference between stoss and repeated groups significant ($0.01 > P > 0.005$).

mortality tended to occur when the reinfecting dose was lighter. There was, however, one exception to these general findings, and that was in experiment 3a, in which the repeated group showed a lower mortality than the stoss group when reinfecting. The difference was not significant at the 5% level, and it occurred only once out of a total of 13 experiments.

It had been hoped at the onset that more clear-cut differences might have been obtained in each individual experiment, but the difficulties inherent in the nature of the experiment prevented this. The mouse is highly susceptible to pneumococcal infection, and therefore, under these conditions, mortality is a crude end-point. The success of each experiment depended not only on reinfection but on careful preliminary preparation by the primary infection together with its treatment. When immunity was sufficiently high, evaluation by mortality was not sensitive enough and would therefore not allow differentiation between the two treatment groups in every experiment. Finally it was not possible to handle more than 150 animals in each experiment; had larger numbers been used, greater differences might have been obtained. Nevertheless, in 10 out of 13 experiments, the mortality in the stoss group on reinfection was less than in the repeated group; in two of these ten experiments (5a and 5b) this difference was significant at the 1% level. It is unlikely that the lower figures for mortality in the stoss group in the remaining eight experiments were the result of chance, since in each experiment the trend was in the same direction. Moreover, when the results of all experiments were added together, the difference between survival in the two groups was significant at better than the 1% level in favour of stoss therapy (Table IV).

It is difficult to explain why those mice previously treated with a single dose should be more immune than those treated by multiple doses. A possible explanation might be that after the large single dose was no longer therapeutically active the damaged organisms and possibly "persisters" (Bigger, 1944a) which remained started dividing and again stimulated the response of the immune mechanism; the latter had already been stimulated when the animals were infected and treatment delayed for 10 hours, so that, although the time interval was very short, this was in the nature of a "booster" dose.

Size of Reinfecting Dose

It has been mentioned before that, except in experiment 1a, all reinfecting doses were of two strengths; this was done in order to increase the chances of discovering a difference in mortality. That this was of value was shown in experiments 2a, 3a, and 6a, in which the stronger dose revealed a difference in mortality which the weaker dose had failed to show.

Primary Infection

The results of primary infection revealed that in some of the experiments more mice in the stoss group died than in the repeated group; this was expected. It was, however, surprising that in three experiments (representing 150 mice) no deaths in the stoss group were recorded; this was achieved with only a single dose of chemotherapy, which had been delayed 10 hours after the onset of infection.

These low mortality rates might have been partly due to the contribution of the host. There is some evidence that this occurs in varying degrees. Thus Buck and Schnitzer (1945) showed that the combination of effective doses of antipneumococcal serum with subtherapeutic doses of penicillin exerted a striking synergic effect in mice infected with pneumococci. Rammelkamp and Kirby (1945) thought that the development of natural immunity was probably important in pneumococcal infection. Evidence in a negative sense was provided by Skinsnes and Woolridge (1948), who showed that protein depletion adversely affected the removal of pneumococci from the host's tissues. However, Florey (1952) has said that she does not consider that the natural antibacterial mechanisms can be taken into account

in determining dosage of penicillin. It is known that specific defences are not necessary for some therapeutic successes with penicillin. For instance, Harrison (1946) abolished the immune response of highly immunized rabbits and mice with excess soluble antigen and showed that this abolition did not alter the effectiveness of penicillin. This might, however, have been due to the overwhelming effectiveness of the penicillin, and, had the dosage of that antibiotic been smaller, a difference might have been revealed.

Fate of Original Controls

The survivors of the primary infections in the control group were reinfecting 10 days later at the same time as the other groups. This was done in order to compare the mortality of these original controls with that of the treated groups. It was possible to do this in only four of the experiments, as the mortality of the controls in the remainder was so high that either no mice or only a few were alive for reinfection. The fate of these controls is shown in Table VI.

TABLE VI.—Fate of Original Controls

Experiment	No.	Primary Infection Survivors	Deaths, Reinfection
1	50	33	18
2a	25	14	4
2b	25	14	0
3a	30	13	3
3b	30	13	0
4a	25	7	5
4b	25	7	3
Total ..	210	101	33

In experiments 1 to 4b about one-third (33 out of 101) of the survivors in the original control group died on reinfection. When the mortality figures for the stoss and repeated groups were calculated in the same experiments, it was found that 49% and 56.7% of the survivors died (Table VII). In these experiments there is a gradation in

TABLE VII.—Fate of Survivors of Primary Infection on Reinfection

	Survivors of Primary Infection	Deaths from Reinfection	Percentage Mortality
Original controls ..	101	33	33
Stoss ..	203	100	49
Repeated ..	208	118	56.7
New controls ..	210	188	90

mortality when the latter is expressed as a percentage of survivors of the primary infection. Thus the most immune group were the original controls with a mortality of 33%, then the stoss group with 49% and the repeated group with 56.7%; and finally the new controls with a mortality of 90%.

The above figures suggest that the original controls—that is, those never treated—once they had survived the primary infection were much more immune (at the 1% level of significance) than either of those groups whose infection had been effectively treated before by chemotherapy.

The present findings in this respect may be similar to those reported by Pratt (1955) and by El-Rooby and Gohar (1956); these workers showed that, in treating typhoid fever with chloramphenicol, the earlier the treatment the higher the relapse rate. That delay in the treatment of pneumococcal infections with chemotherapy allowed a higher immunity to develop was well shown in Harrison's (1946) experiments in mice and rabbits. The longer treatment was delayed the greater the subsequent development of immunity, which was, however, accompanied by a greater immediate mortality.

In clinical practice, although the problem is twofold, attention is usually focused on only one aspect, the optimum treatment, and not on subsequent immunity. This is mainly because we are unaware of many of the factors causing recurrence of disease and uncertain of the part played by

chemotherapy in this respect. In a study of recurrences in pneumonia Strauss and Finland (1942) have shown that in those cases treated with sulphonamide there was a greater tendency for attacks to recur at shorter intervals, and for the same type of pneumococcus to occur more frequently in both attacks, than in those treated with serum or non-specific therapy. On the other hand, Jordan *et al.* (1950) have shown that, in any event, by the time the patient has symptoms the immune response has already been stimulated, and indeed that this response (measured by agglutination titres) was no different in those treated and those not treated by chemotherapy.

The present work in mice suggests that there is some difference in the degree of immunity developed, depending on the method of treatment when using the same drugs. Under the conditions of these experiments, the subsequent immunity was greater following stoss-therapy than that following the repeated treatment.

Now that chemotherapy is so effective in the treatment of numerous infections, we should, I suggest, take into consideration the more remote and long-term factors as well as the immediate effect of treatment. In this way prevention as well as cure may be achieved.

Summary

As a result of the good response observed in children with acute respiratory infection when treated with a single dose of penicillin and sulphadimidine (stoss-therapy), an experimental investigation into the relationship between method of treatment and subsequent immunity was planned.

The experiments were designed to investigate the immunity of mice which had been infected with virulent pneumococci and then treated with a mixture of sodium sulphadimidine and penicillin. There were two different treatment groups: (1) a single massive dose of sulphadimidine and penicillin (stoss-therapy), and (2) six smaller doses repeated at intervals of eight hours. Treatment of both groups was delayed 10 hours after infection. Ten days later the survivors in each group were reinfected with challenging doses of pneumococci, and the immunity of each treatment group was evaluated by mortality.

In each experiment except one the single-dose group (stoss) showed either a lower or a similar mortality on reinfection compared with the group having repeated doses. When all the results were taken together, a significant difference at the 1% level in favour of stoss-therapy was observed.

So far as these results can be applied to natural human infection, the greater immunity of the stoss-treated group over the repeated-dosage group offers a further reason for using stoss-therapy in suitable cases of human pneumococcal infection.

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SPLenic ARTERIAL ANEURYSM

BY

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Aneurysm of the splenic artery was mentioned by Beaussier in 1770. Winckler (1905) recognized the condition in the living, Höglér (1920) made the diagnosis before operation, and Lindboe (1932) was the first to make a radiological diagnosis. Perhaps the most famous example was that of President Garfield, who died from a ruptured traumatic aneurysm of the splenic artery two months after being shot by an assassin.

Splenic arterial aneurysm is a rare condition, and rupture is usually fatal. Owens and Coffey (1953) reviewed 204 fully documented cases, and Hill and Inglis (1955) found 35 survivors after surgery, including only nine after rupture. A further four recoveries after rupture have been reported by Gallagher and Hudson (1954), Parrella (1955), Colangelo (1955), and Owen, Holmes, and Scannell (1957). Among these 13 survivors after rupture were four pregnant women (Owen *et al.*, 1957).

Diagnosis before rupture is uncommon (Hughes and Joske, 1955; Riemenschneider, 1955). Berger, Forsee, and Furst (1953) considered their case to be the eleventh diagnosed before operation in the English literature.

There are many unrecorded cases of splenic arterial aneurysm, particularly those seen at necropsy, and those diagnosed radiologically and not confirmed by operation.

The purpose of this paper is to discuss five patients with splenic arterial aneurysms operated on in Mansfield during the past two years. Four of the five survived. In two the aneurysm had ruptured; one, a pregnant woman with a porto-caval shunt, recovered. The other three were diagnosed on radiological grounds before operation. In two the operative removal was incidental to that of a carcinoma—of the oesophagus in one, and of the kidney in the other. The remaining patient had urological symptoms and hypertension, but none referable to the region of the aneurysm.

Case 1. Staged Rupture—Splenectomy—Death in Anuria

A publican of 42 was admitted as an emergency case with pain in the left hypochondrium. A severe attack of pain in the left loin passing to the left chest in the mid-axillary line,