peutic agents: twenty-two of them are nearing the end of their treatment. The methods employed and illustrative cases are recorded. The tabulated conclusions provide a basis for an extended trial of these methods as a first-aid measure in the prevention of shock and the control of infection and as a method of treatment in selected cases. The possibility of replacing dressings and rubber tissue by one portable and easily sterilizable substance is suggested. Stress is laid on the necessity and facility for early painless rehabilitation of the wounded.

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THE VALUE OF THE NON-SPECIFIC FACTOR IN EXPERIMENTAL IMMUNIZATION WITH INFLUENZA VIRUS

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Influenza is one of the few virus diseases which do not induce in the patient after recovery any manifest immunity, although during and after convalescence virucidal antibodies can be detected in the serum. After a few months have elapsed a second attack may be experienced. As there is only a transitory immunity after recovery from the illness, the possibility of acquiring more prolonged immunity by artificial immunization is very limited.

So far laboratory experiments on ferrets and mice show that it is possible to immunize these animals for a period of about three months only if the virus is applied intranasally. If at the end of that time the virus is injected subcutaneously, immunity can be prolonged over a further period, as shown by the resistance of the ferrets to reinfection by the nasal route (Laidlaw and others, 1935). The only positive effect in the immunization of ferrets and mice by routes other than nasal is an increased resistance in the immunized animals to lung lesions caused by the subsequent application of influenza virus; this may be due to the presence of protective antibodies induced by the previous injection of the virus.

In the blood of immunized animals and in human beings after recovery there can be demonstrated virucidal, precipitating, and complement-fixing antibodies (Magill and Francis, 1938; Hare, 1939; Fairbrother and Martin, 1939; Eaton and Beck, 1940), but their immunizing effect, as demonstrated by insufficient subsequent protection against reinfection, is disappointing in most cases. One possible explanation of this inadequacy is the fact that there are several types of influenza virus; but, on the other hand, these are antigenically very close, as they give a cross-complement-fixation with each other.

Unfavourable reports on the immunization of human beings with the vaccines at present available have been published in this country and in the U.S.A. (Dochez, Mills, and Kneeland, 1938; Powell, Sparks, and Clowes, 1940; Stuart-Harris, Smith, and Andrewes, 1940; and others). The

new combined influenza and distemper virus vaccine introduced by Horsfall and Lennette (1940a, 1940b) seems to be promising, but results are not yet available.

As the usual influenza virus suspensions do not give satisfactory (that is, only transitory) results when applied by routes other than the nasal, we tried to increase specific immunity by adding to the specific stimulus an unspecific factor which would activate the reticulo-endothelial system, or act by simultaneous local irritation of the tissues. This method is often successfully applied in immunization against bacteria and their toxins, and therefore a trial in the case of the influenza virus was logical.

The following experiments were carried out:

Experiment 1

Groups of 50 mice from one stock were given subcutaneous injections of 0.25 c.cm., 0.25 c.cm., and 0.5 c.cm. at weekly intervals of the following three preparations:

- (a) A vaccine containing per c.cm.:
<i>B. pneumoniae</i> (Friedländer)	25 millions
<i>M. catarrhalis</i>	25 "
<i>Pneumococcus</i>	150 "
<i>Streptococcus</i>	150 "
<i>Staphylococcus</i>	100 "
<i>C. coryzae</i>	25 "
<i>H. influenzae</i>	100 "
Preservative, 0.5% phenol	
- (b) A vaccine containing per c.cm.:
<i>Sarcina</i>	3 millions
<i>B. mycoides</i>	2 "
<i>Pneumococcus</i>	1 million
<i>Streptococcus</i>	1 "
Mixed lipoids (cod-liver oil, 0.02 mg.;
cholesterol, 0.67 mg.; lecithin,
0.1 mg.)	0.187 mg.
Preservative, 0.5% phenol	
- (c) Saline containing 0.5% phenol

Three weeks after the last injection the mice received 0.05 c.cm. of a suspension of influenza virus Type A prepared as follows:

Lungs were removed from mice which had been infected with the virus five days earlier. The lungs were weighed moist, pulped in a mortar, and taken up in broth in the proportion of 2.25 grammes to 10 c.cm. This suspension was centrifuged and filtered through a small Berkefeld candle. The filtrate showed high activity of the virus, as mice were killed by intranasal instillation of dilutions of 1 in 1,000. The injections were made intranasally under chloroform-ether anaesthesia. Ten normal mice were similarly injected at the same time to serve as additional controls.

The results from the three preparations were: (a) 6% survivals, (b) 12%, (c) 11%. Survivals from the controls amounted to 20%.

Experiment 2

A suspension of influenza virus prepared as described above, except that saline was used instead of broth, was incorporated in the following preparations:

- (d) A mixture of preparation (a), 2 parts; mixed lipoids as in (b), 1 part; influenza virus, 1 part
(e) Mixed lipoids, 3 parts; influenza virus, 1 part
(f) Colloidal calcium, 3 parts; influenza virus, 1 part
(g) Saline, 3 parts; influenza virus, 1 part

0.1% formalin was added to all the mixtures, and they were kept in the refrigerator pending animal experiments.

Groups of 24 mice were given subcutaneous injections of 0.25 c.cm., 0.25 c.cm., and 0.5 c.cm. at weekly intervals. One week after the third injection they received 0.05 c.cm. of a suspension of influenza virus intranasally under chloroform-ether anaesthesia.

The results from the four preparations were: (d) 87% survivals, (e) 96%, (f) 79%, (g) 88%.

Conclusions

From the above experiments it is evident that the immunization of mice against bacteria associated with cold infection has no protective effect against subsequent infection with influenza virus. Mice immunized either with a cold vaccine or with a polyvalent antigen show the same

percentage of deaths as the mice injected with phenolized saline.

Having excluded the possibility of the production of non-specific immunity by bacteria, we found in the second experiment that there was no substantial difference between the resistance of animals in the four groups to subsequent infection with influenza virus.

These experiments indicate that the simultaneous application of heterogeneous substances had no influence on the production of immunity against influenza virus.

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THE CONTROL OF GASTRIC HYPERACIDITY IN PEPTIC ULCER

BY

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In spite of all attempts to discover the aetiology of chronic peptic ulcer it must be admitted that the essential cause still eludes us. Analysis of the gastric juice frequently shows a high acidity, less commonly a moderate or low one, but a total absence of hydrochloric acid is quite unknown in this condition. While we have often concluded that hyperacidity is a cause of gastric ulcer, we have no evidence in favour of this at all. There is more evidence that the presence of HCl tends to continue the activity of an ulcer, once it has formed, and that healing is prevented. For this reason, chiefly, our main attempts at therapy in peptic ulcer have hitherto centred on the continuous neutralization of HCl by diet, drugs, and other methods. Quite probably the acid factor is not the sole cause of an ulcer's not healing, but at present the neutralization of HCl is our main therapeutic weapon. Furthermore, it is already clear that ulcers do heal even when HCl is present in the stomach during part of each day.

Diet as a means of neutralization of acid takes first place, and is given at hourly or at most two-hourly intervals; but it is already known that this cannot bring about continuous neutralization, and, moreover, during the hours of sleep feeding is impossible. Numerous drugs (alkalis and others) have therefore been used, but they are in many ways unsatisfactory. We want to find, if possible, foods or simple drugs that will ensure continuous neutralization throughout the twenty-four hours, or will keep the secretion of HCl permanently as low as possible.

The series of experiments now to be described were undertaken with a view to discovering the most suitable foods or simple drugs to maintain neutralization for as long as possible during the twenty-four hours. The substances under investigation were given two-hourly, and the stomach contents in all cases were examined repeatedly during a continuous period of twelve hours, the Ryle tube

being kept in position; samples were removed for hourly examination shortly before and one hour after feeds. All patients included in this investigation presented clinical and radiological evidence of peptic ulcer, and fractional test meals were first given in the usual way, with oatmeal gruel as the stimulant of gastric juice. Every test showed hyperacidity, and the curves obtained over two and a half hours were in general similar to those described by Ryle (1921).

Methods of Titration

The amounts of fasting juice and residue were measured, and all specimens were titrated for free and total acidities with decinormal sodium hydroxide, using methyl orange and phenolphthalein as indicators respectively. Results are expressed as units in terms of c.cm. N/10 NaOH required to neutralize 100 c.cm. of fluid. Only the free-acid readings are here recorded.

Group I (9 Cases)

For purposes of comparison feeds of milk, 10 oz. by mouth, were used in each case before other treatment. Parallel experiments with whole milk and citrated milk indicated no appreciable difference between the two in the resultant acid level, and as the thick clots of whole milk were found to block the tube the work was continued with citrated milk, to which alone results refer. Considering the great importance attached to milk in the treatment of peptic ulcer, one would expect to find that it caused a substantial reduction of acidity. But Nicol (1939) could not demonstrate this either by two-hourly or by hourly feeds; indeed, he recorded a higher acidity with milk two-hourly than with a diet consisting of three full meals. By quarter-hour readings he showed that a fall occurred immediately following each feed, but only of short duration: before the next feeding-time the level had risen to its previous height. The results of the present experiments are in complete agreement with those of Nicol. Surprisingly high levels were obtained: it was common to find figures of total acidity of 70 to 80 units, and few were below 30. The charts, with hourly readings, did not show the fluctuations indicated by Nicol, but the reference is the same—namely, that milk given at two-hourly intervals has little if any continuous antacid value.

Gelatin (feeds of 10 oz.) was next used, prepared according to the method of La Due (1939)—gelatin 1 part, lactose 3, water 32 parts. Andresen (1927, 1939) used this mixture with success in the treatment of haematemesis. I had already tried it as a secretory stimulus in the fractional test meals of 7 patients and had compared the results with those of gruel meals in the same cases. Apart from the fact that gelatin specimens were homogeneous and easier to titrate, no significant differences were noted in the acid curves; similarly, in the twelve-hour tests gelatin appeared to have approximately the same neutralizing power as milk, although the former is supposed to be a powerful stimulant of gastric juice.

The rational use of olive oil in the treatment of peptic ulcer is demonstrated in this series; both olive oil and peach-kernel oil were found to cause a substantial reduction of acidity, an effect already reported by Roberts (1931). In 4 cases three feeds of milk (10 oz.) were given two-hourly followed by three of oil (2 oz.) two-hourly; and in the second half of each test there occurred a fall of 20 to 60 units. The experiments were repeated several times in the reverse order, and a similar depression with oil was followed by a rise to over 40 units under the influence of milk. Chart I represents such curves, obtained from one patient. Peach-kernel oil and an emulsion of olive oil, as will be observed from Table I, are not quite so effective as undiluted olive oil. A criticism was offered that the low acid values were due to the nauseating taste of oil; but this was disproved by the fact that when oil was syringed down the Ryle tube the values were even lower than when it was given orally.

As a deliberate contrast tests were made with two substances which are supposed to be strongly acid-producing—bovril and strained meat stock. The latter has always been excluded from the dietary regimes of dyspeptic patients; but, as Table I shows, from the point of view of acidity this is an