

presenting themselves to him in the social service field. We might well consider the economic phase of this question from the medical standpoint. We are reducing incomes in the profession 30 to 40 per cent. by medical preventive work, and we should plan to take care of the physician who has cooperated in reducing his work and thereby his income.

## A METHOD OF SELECTION OF DONOR FOR BLOOD TRANSFUSION \*

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The possibility of iso-agglutination makes the choice of a donor for blood transfusion an important matter. It has been shown that individuals fall into definite groups as regards this phenomenon, and only a person belonging to the same group as the patient who is to be transfused should be selected as donor. It is obvious that it is unsafe to transfuse with the blood of a donor whose serum will agglutinate the patient's corpuscles, or whose corpuscles are agglutinated by the patient's serum, and still more so when both these reactions occur. Cases with seemingly unfavorable results under these conditions have been reported by Schultz,<sup>1</sup> Ottenberg<sup>2</sup> and Hopkins.<sup>3</sup>

The following method may be used for carrying out such tests: So far as the blood of the donors to be tested is concerned, sufficient blood may be obtained from the ear; but in the case of the patient it would be better to draw the blood from the median basilic vein of the arm in the usual way because more serum is required. Three drops of the blood are added to 10 c.c. of a 1 per cent. solution of sodium citrate in physiologic salt solution. In this manner approximately a 2 per cent. suspension of the blood is prepared, the citrate preventing coagulation. The remaining blood is poured into a centrifuge tube and allowed to clot. With a clean needle the clot is loosened from the side of the tube and the tube centrifuged for a few minutes to obtain an upper layer of absolutely clear serum. This completes the preparation of material, with the exception of the plate which is now to be described and which has been found to be very serviceable. On an ordinary piece of window glass, approximately 2 by 4 inches in size, which has been washed absolutely clean with water and ether, ten small circles are made with melted paraffin, assuming that a choice is to be made among five donors. If the melted paraffin is drawn up into a medicine-dropper, the circles are quickly made with the tip while gentle pressure is exerted on the bulb. Ten circles may be made with one medicine-dropper full of melted paraffin. In this manner ten paraffin cups are made, each of which will hold at least 4 drops. The circles are made in two rows of five each. In each cup in the first row is placed 1 drop of the suspension of the patient's blood, and in each cup in the second row are placed 2 drops of the patient's serum. To Cup 1 in the first row are added 2 drops of serum of Donor 1, to Cup 2, 2 drops of serum of Donor 2, etc. To Cup 1 in the second row is added 1 drop of the blood of Donor 1, and to Cup 2, 1 drop of the blood of Donor 2, etc. There are therefore required in

such a set 5 drops of patient's blood suspension, and 10 drops of patient's serum, and 1 drop of each donor's blood suspension and 2 drops of serum. With a narrow glass rod the fluids are mixed thoroughly, the rod being washed in citrate solution and wiped after each mixing. In practically all instances, iso-agglutination when present becomes visible macroscopically after half an hour at room temperature; the mixture can be inspected easily under the microscope also. It is obvious that in testing for iso-agglutination in larger groups, as in twenty, the greatest advantage is to be derived from this method. It has seemed so simple and easy of performance in comparison with other methods that it was thought best to make a brief report of it.

## THE PALLIATIVE TREATMENT OF TERMINAL LARYNGEAL TUBERCULOSIS \*

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The palliative treatment of terminal laryngeal tuberculosis is a thankful one. In private practice, much can be done by daily treatments to relieve the severity of the patient's sufferings, but in institutional work the problem is entirely different. In public hospitals, as a rule, it is unusual to have a trained laryngologist constantly in attendance. Therefore the questions arise what practical methods should be adopted for giving permanent relief from the laryngeal pain, and whether such methods could be put into the hands of the resident physician. Whether this problem has been solved can be determined by a study of the results obtained in the following series of cases.

The condition of these patients is such as to awaken our deepest sympathy. Doomed in a few months to die, with absolutely no hope of escape, their last moments are made miserable by continuous pains in the larynx, which are present not only during the ingestion of food, but even when the larynx is in a condition of rest. The taking of solid food is an impossibility; and even the swallowing of water or milk produces such an agony of suffering that slow starvation is generally preferable.

Local applications of cocaine, frequent insufflations of propaesin, anesthesin or orthoform, local cauterization with lactic acid, can all be used with marked benefit to the patient. As a usual thing, however, these measures give only temporary relief and in addition consume so much time as to make them impossible to be thoroughly carried out in a hospital of several hundred beds.

In the cases which are not too far advanced, the patient can be instructed in methods of auto-insufflation, but in the bed-ridden patients, in whom the suffering is the most intense, local methods have been found to be of very little benefit.

It occurred to Rudolf Hoffman, of Munich, that some form of permanent anesthesia of the interior of the larynx would prove an unbelievable blessing to this class of poor unfortunates. The brilliant results in superficial neuralgias, which followed Professor Schlösser's original communication on the use of alcohol injections in these conditions, gave him the clue, and he saw that by injecting the superior laryngeal nerve such an anesthesia might be brought about. Already Braun and Frey, by means of cocaine injections in the region of

\* From the Memorial Institute for Infectious Diseases.  
1. Schultz: Ueber Bluttransfusion beim Menschen unter Berücksichtigung biologischer Vorprüfung, Berl. klin. Wchnschr., 1910, xlvii, 1407.  
2. Ottenberg: Transfusion and the Question of Intravascular Agglutination, Jour. Exper. Med., 1911, xlii, 425.  
3. Hopkins, J. Gardner: Phagocytosis of Red Blood-Cells After Transfusion, Arch. Int. Med., September, 1910, p. 270.

\* Read before the San Francisco Polyclinic Society, June 5, 1912.

the ramus internus of the superior laryngeal nerve, had secured anesthesia sufficient to carry out small laryngeal operations.

The emaciation which is usually an accompaniment of tuberculosis in the latter stages makes it particularly easy for this procedure to be carried out successfully. The point of entrance of the nerve through the thyrohyoid membrane can be palpated with great exactness. The technic of making the injection is as follows: The skin is first prepared by painting the region to be injected with iodine. The left side of the larynx is grasped with the first and second fingers of the right hand, and with the thumb of the same hand the painful point is located. As soon as this spot is found the thumb-nail is pressed in to mark the spot and the needle is introduced at that point. The needle is introduced perpendicularly for 1.5 cm.; then the point is moved in all directions until a sharp pain, radiating to the ear, is felt. From 3 to 5 c.c. of a warm solution of 85 per cent. alcohol are then injected until the pain in the ear disappears. The point of entrance of the nerve will be found just at the upper edge of the thyroid cartilage, about one-third of the distance from its outer edge.

In none of the sixteen cases reported by Hoffman, and certainly in none of my own cases, were untoward effects observed. In fact, it can be stated that the procedure is entirely without danger. The relief from pain is immediate, and aspiration of food as a result of paralysis has seldom been observed. The injection can be repeated without danger as often as necessary. The duration of the anesthesia varies from a few hours to as long as forty days.

To my mind one of the most important secondary effects of the injection is the mental effect on the patients. The immediate relief from pain gives them hope of rapid recovery; their spirits improve and they try to take more nourishment.

The great value of this procedure is undoubted, yet a study of the literature shows surprisingly few case series reported. The simplicity of the procedure, the ease of application, the permanency of the result, and, most important of all, the fact that the method can be used by any medical man or intern, make it a relief measure with which every man working with tuberculosis should be familiar.

The tabulated series of cases, studied at the San Francisco City and County Hospital for Tuberculosis, is especially interesting for several reasons, and as far as the literature shows, absolutely unique, in that only those cases were selected in which death was inevitable within a few weeks, and the sufferings of the patients were intense. The majority of the patients found the greatest relief from pain and surcease from their sufferings up to the day of their death. The negative results in three cases are self-explanatory.

The negative results in the series mentioned above, and in some subsequent cases in which the laryngeal involvement was not so marked, bring out one interesting point. If there is an involvement of the epiglottis, especially on the external surface, the relief from the injection is entirely absent in most cases, and only partially present in others.

TABLE SHOWING RESULTS OF ALCOHOL INJECTION IN TEN CASES OF TERMINAL LARYNGEAL TUBERCULOSIS

No.	Name	Sex	Age	Pulmonary Findings	Larynx Findings	First Injection	Condition Before Injection	Relief After Injection	Days After Injection	Later Injection	Condition Before Second Injection	Death	Total Days Relief
1	N.	M.	35	Very late cavity formation; daily fever.	Both cords and arytenoids deeply ulcerated; epiglottis free.	2/1/12 Both sides.	Continuous pain, night and day; increased on swallowing.	Immediate relief; freedom from pain; eating and mental condition improved.	30	Second. 3/2/12	Patient rapidly failing; mentally irrational; complains of some pain.	3/18/12	46
2	K.	M.	23	Same as Case 1.	Filled with pus and mucus; ulceration of arytenoids.	2/4/12 Both sides.	Continuous pain, night and day; solid food impossible; takes milk, one swallow at a time.	Great relief, lasting until death.	14	None.	.....	2/18/12	14
3	W.	F.	55	Same as Case 1.	Large ulceration of tongue and in arytenoid space; fungating granuloma of right cord; large ulceration of septum.	2/1/12 Both sides.	Sharp, racking, continuous pain, day and night; cannot drink milk or water except by single swallow.	Immediate, marked improvement; free from all pain; swallows easily; takes solid food; says relief is wonderful.	3	.....	Repetition of injection not absolutely necessary, but was made at request of patient; comfortable up to death.	3/3/12	31
4	C.	M.	25	Same as Case 1.	Large ulcerative process of cords and arytenoids.	2/12/12 Both sides.	Great pain on swallowing and between meals.	Immediate marked improvement; drinks an entire glass of milk.	31	3/15/12	Pain has returned last few days; patient wants second injection.	3/16/12	31
5	B.	M.	32	Same as Case 1. Tuberculosis of femur.	Slight infiltration of interarytenoid space; no ulceration.	2/28/12 Both sides.	Complains of constant backing cough; no pain on swallowing.	Immediate relief from cough, which patient ascribes to injection (?).	19	.....	.....	4/24/12	†
6	S.	M.	27	Patient in extremis; rapidly failing.	Filled with pus; regurgitates all food.	2/19/12 Both sides.	Constant pain on swallowing.	Relief claimed by patient, who is not rational; result considered doubtful.	..	Second injection refused.	.....	5/29/12	†
7	H.	M.	47	Same as Case 1.	Great thickening of epiglottis; no view of larynx.	3/21/12 Both sides.	Burning pain on swallowing; can take no liquids.	Relief after forty-eight hours.	9	None.	.....	3/30/12	9
8	W.	F.	36	Same as Case 1. Weight 69 lbs.	Large ulceration of arytenoids; first exam. 3/6; no pain till 3/28.	3/28/12 Right side.	Pain on swallowing.	Relief immediate and lasted until death, April 11, 1912.	15	None.	.....	4/11/12	15
9	D.	M.	56	Same as Case 1.	Cords, arytenoids and epiglottis ulcerated.	3/19/12	Continuous and racking pain; demands relief by repeated injections.	Nerve not located by first two inj.; immediate, marked relief following third.	34	2nd. 3/28; 3rd, 4/11/12	.....	5/15/12	34
10	Y.*	M.	37	In extremis.	Extensive ulceration of cords and arytenoids.	4/4/12 Both sides.	Continuous racking pain.	Nerve not located; no pain in ears; no relief.	†	.....	.....	4/4/12	..

\* Japanese. † Died day of injection. ‡ Relief from injection doubtful.

This fact was proved in one case in which the ulceration involved the internal surface of the epiglottis. Because of its low position it was thought inadvisable to amputate. Repeated alcohol injections were made both by myself and others without the slightest relief. Subsequent amputation of the epiglottis gave immediate and lasting relief. This is probably to be explained by the fact that the external surface of the epiglottis is innervated by the glossopharyngeus, while the internal surface is innervated by the superior laryngeal nerve coming from the vagus.

The severity of the cases can be appreciated by the fact that the longest period a case was under observation before death intervened was forty-six days; the shortest, three days. The relief in most cases was immediate and marked, lasting usually up to the day of death. Most of the patients requested a second injection and described the relief in the most exaggerated terms such as "marvelous," "wonderful," etc.

The accompanying table is self-explanatory. All of the patients were bed-ridden; none recovered. Although this procedure can in no sense be looked on as a curative measure, the marked relief afforded the patients puts it in a class by itself as a palliative measure.

In conclusion, it should be noted that the failures are, in the vast majority of cases, due to faulty technic. This can usually be proved at the time of the injection. If the patient does not complain of a sharp pain, due to a rubbing of the point of the needle against the nerve, the injection will probably be a failure. It is always well, however, when it has been impossible to locate the nerve by this method, to inject the alcohol, as the perineural infiltration will possibly cause enough anesthesia to help the patient greatly.

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## IMMUNIZATION IN PNEUMOCOCCUS INFECTIONS \*

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The formation of antibodies in those infections due to bacteria which produce little or no soluble toxins is held to be due to the stimulus of the whole bacterium in question. Intoxication and immunization are held to be due to the same cause. The idea that there are produced during infections substances purely toxic in nature which do not call forth an immunizing response, but which may even interfere with the proper formation of antibodies in response to certain other substances, has not been considered by most investigators.

In this paper I wish to present briefly the results of immunization experiments in animals and the results of the treatment of lobar pneumonia in man with various products obtainable from pneumococci.

The opsonic content of the serum in lobar pneumonia has been found to be below normal during the early part of the disease, but well above normal as the symptoms subside. In those patients who die from overwhelming infection it remains persistently below normal. In experimental pneumococcus infections the opsonic curve runs a similar course. When pneumococci killed by heat are injected there is first a reduction and then an increase in opsonin practically similar to what occurs

during an infection. The opsonic content of the serum for pneumococci may therefore be looked on in a general way as an index of resistance.

When highly virulent pneumococci are allowed to autolyze in sodium chlorid solution there appears at a certain period a highly toxic substance. This, when injected intravenously in guinea-pigs, rabbits and dogs, produces symptoms characteristic of anaphylaxis in these species, and when injected subcutaneously in man produces a moderate increase in opsonins after a short negative phase, rather marked local reaction, leukocytosis and some fever. These extracts call forth reactions in man similar to those caused by the heat-killed bacteria. The pneumococci after extraction or autolysis lose the ability to retain the Gram stain, show varying degrees of disintegration, and when injected into animals and man exert little or no toxic action, but induce a prompt rise in the opsonic power of the serum without a preceding negative phase. By injecting large enough doses of a combination of the toxic material and the autolyzed pneumococci I have been able to produce a continuous negative phase similar to that observed in overwhelming pneumococcus infections. The mechanism of immunization seems paralyzed. In this connection it should be pointed out that the action of the toxic material obtained by autolysis of pneumococci is exactly similar to that which I have found in various pneumococcus exudates, such as the peritoneal exudate in pneumococcus peritonitis from the consolidated lung in pneumonia, from pneumococcus empyema pus, etc. The appearance of the toxic material in pneumococcus extracts and its disappearance have been found to be associated with proteolysis. The toxicity of the extracts may be temporarily restored by the addition of serum, but not by a second addition of serum. It has been found that intravenous injections of heat-killed pneumococci, of pneumococcus extracts during the toxic stage and after the toxicity has disappeared, of pneumococcus broth-culture filtrates and of autolyzed pneumococci render guinea-pigs resistant to subsequent injections of toxic autolysates in two, four, six, twenty-four and forty-eight hours, respectively. Salt solution, broth and extracts of typhoid bacilli, on the other hand, do not render guinea-pigs refractory to toxic pneumococcus autolysates. The reaction seems to be specific. The facts that the extracts after they have lost their toxicity and that autolyzed pneumococci which are non-toxic call forth reactions which render guinea-pigs resistant to such highly toxic material speak in favor of the view that intoxication is not essential in this process, but without further proof we could not be sure but that a certain amount of intoxication follows even these non-toxic injections.

The highly toxic substance in pneumococcus autolysates has been found to be soluble in ether. This serves to separate the toxic substance from the protein constituents of the autolysate. The ether-soluble material produces symptoms in guinea-pigs exactly similar to those observed following the injection of the autolysate itself, but fails to render the animals insusceptible to subsequent injections of both the toxic autolysate and the ether-soluble portion. We have here then an example of intoxication by a bacterial product which does not call forth an immunizing response. Moreover, the protective value against experimental pneumococcus infections in the guinea-pig and rabbit, of heat-killed pneumococci and of pneumococcus extracts before the toxic stage has been reached has been found to be distinctly less than that of large doses of autolyzed pneumococci

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\* From the Memorial Institute for Infectious Diseases, Chicago.