

A REPORT ON FORTY CASES OF ACUTE ARTHRITIS
TREATED BY THE INTRAVENOUS INJECTION
OF FOREIGN PROTEIN *

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Nonspecific vaccination in the treatment of infections is not a new procedure. As far back as 1893, Rumpf¹ treated typhoid fever patients with a *B. pyocyaneus* vaccine and claimed to have obtained excellent results. Von Wagner² found that paretics treated with tuberculin showed marked improvement. Hiss and Zinsser³ used extracts of rabbit's leukocytes in various infectious diseases, especially pneumonia, and were favorably impressed with the results. Some of the German writers have employed boiled milk subcutaneously in infections, and report success. More recently Schaefer's mixture of many bacteria has been widely advertised in the treatment of various diseases, more particularly of arthritis.

The practice of intravenous injection of foreign proteins is a comparatively recent one, and may be said to have originated with the intravenous injection of typhoid vaccine in the treatment of typhoid fever. Ichikawa⁴ was one of the first to use the intravenous method of vaccination. By giving sensitized typhoid vaccine intravenously he observed that cases not only of typhoid but also of paratyphoid fever often showed marked improvement after the injection, the temperature sometimes dropping to normal and remaining there. Gay and Chickering,⁵ Miller and Lusk⁶ and others have reported favorably on the results of intravenous injections of typhoid vaccine in typhoid fever. Kraus⁷ obtained similar results in typhoid fever by using colon bacillus vaccine intravenously. Lüdke⁸ substituted albumose for vaccine and obtained the same sort of a crisis in many cases. Psoriasis and certain other skin diseases have been successfully

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1. Rumpf: Deutsch. med. Wchnschr., 1893, **19**, 987.
2. Von Wagener, J.: Wien. med. Wchnschr., 1909, **59**, 2124.
3. Hiss, P., and Zinsser, H.: Jour. Med. Research, 1908, **19**, 321.
4. Ichikawa, S.: Ztschr. f. Immunitätsf., 1915, **23**, 32.
5. Gay, F., and Chickering, H.: THE ARCHIVES INT. MED., 1916, **17**, 303.
6. Miller, J., and Lusk, F.: Jour. Am. Med. Assn., 1916, **66**, 1756.
7. Kraus, R.: Wien. klin. Wchnschr., 1915, **28**, 29.
8. Lüdke, H.: München. med. Wchnschr., 1915, **62**, 321.

treated by a number of dermatologists with intravenous injections of serum.

The application of intravenous vaccination to the various forms of arthritis is comparatively recent. Miller and Lusk,⁹ in 1916, reported a series of cases of acute and chronic arthritis in which the patients were treated by intravenous injections of typhoid bacilli and of secondary proteose, and obtained excellent results in a majority of the cases. In a second paper Miller and Lusk⁹ report 85 cases of arthritis in which the patients were treated by the intravenous injection of typhoid vaccine. Forty-five of these were cases of acute arthritis, and 33 of the patients had already been treated with salicylates, without benefit, except in 4 cases. Twenty-nine out of the 45, after receiving one to four doses of vaccine, recovered in one to five days; 8 showed marked improvement, 6 moderate improvement, and 2 no improvement. The 4 gonococcus cases in this series did not respond brilliantly to the vaccine. There were nine relapses in the acute series. Of 12 cases of subacute arthritis, 10 cleared up in three to five days, and the other 2 patients improved. Nineteen chronic but still active cases were treated, in 10 of which the patients showed improvement. Culver¹⁰ reports a series of 31 gonococcus arthritis cases, in 28 of which the patients either recovered or greatly improved after intravenous injection of gonococcus, meningococcus or colon vaccine. Matthers¹¹ reports favorably on various infections, including acute arthritis, treated by intravenous injections of vaccine and pure protein. Manier, Petersen and Jobling¹² have treated 13 patients with arthritis by intravenous injections of secondary proteoses. Three of the cases were acute, 3 subacute and 7 chronic. Of the acute cases, 2 cleared up promptly after the injections, while in the third, a gonococcus arthritis, the patient was not relieved. In the 3 subacute cases the patients all recovered rapidly after vaccination. In the chronic series there was complete relief in 3, marked improvement in 3 and no change in 1. The reports on this subject, though not numerous, have been so favorable that it seemed desirable to give the method a trial.

Classification of Cases.—The present study is based on 40 cases of acute arthritis in which the patients were treated in the medical wards of Bellevue Hospital. These cases may be classified as follows: rheumatic fever, 26; acute toxic arthritis, 7; gonococcus arthritis, 7.

9. Miller, J., and Lusk, F.: Jour. Am. Med. Assn., 1916, **67**, 2010.

10. Culver, H. B.: Quoted by Jobling, THE ARCHIVES INT. MED., 1917, **19**, 1042.

11. Matthers, M.: Quoted by Jobling, THE ARCHIVES INT. MED., 1917, **19**, 1042.

12. Jobling, J. W.: Jour. Am. Med. Assn., 1916, **66**, 1753; THE ARCHIVES INT. MED., 1917, **19**, 1042.

Of the 40 patients, 30 were male and 10 female. The average age of the rheumatic fever patients was 26 years; of the acute toxic arthritis series, 42; of the gonococcus arthritis series, 27. In the rheumatic series 12 patients had been subject to attacks of tonsillitis or sore throat; 15 had had previous attacks of rheumatic fever. In the acute toxic arthritis series only 1 gave a history of tonsillitis and 1 had had a previous attack of the same illness.

Complications.—Tonsillitis was noted as a complication in 8 of the rheumatic fever series; sore throat or coryza in 7 cases; rheumatic endocarditis was noted in 15 cases; pyorrhea was present in 3 of the acute toxic arthritis cases; tonsillitis twice, and pneumonia with empyema, once. In the gonococcus series, 6 of the cases were associated with gonococcus urethritis and 1 with gonococcus vaginitis. In 1 case gonococcus iritis was also present.

The rheumatic fever cases varied in severity. Some of the patients were quite ill, with high fever and profuse sweats. All of the rheumatic fever series were cases of polyarthritis as were also the acute toxic arthritis cases. All but one case of the gonococcus series (Case 40) were polyarticular, but usually the latter changed to a monarticular type.

The temperature on admission varied from 98 to 101 F., but in a few cases it was as high as 102 to 103. The leukocyte count on admission varied from 7,000 to 22,000. Two of the rheumatic fever patients and one of the gonococcus patients had positive Wassermann reactions, but none of these showed any clinical signs of syphilis. The gonococcus fixation test was positive in five out of the seven cases of gonococcus arthritis.

The Vaccine.—Typhoid vaccine has been used almost exclusively in this study. The New York City Board of Health vaccine was employed. It is made up in the usual way from a number of strains of *B. typhosus*. In five of the gonorrheal cases a polyvalent gonococcus vaccine (also New York City Board of Health) was used.

Administration of Vaccine.—The vaccine in every case was given intravenously. The vein used was the median basilic and the injection was made with a small tuberculin syringe. The vaccine was diluted so that 1 c.c. = 100 million bacteria. In none of the cases was there any local reaction. The dose of vaccine administered varied from 30 to 100 million, the usual dose being 40 to 80 million. By a mistake in technic, 400 to 500 million bacteria were given to three patients (Cases 24, 29 and 31). The reaction produced by these large doses was little if any more severe than that caused by small doses, and the therapeutic result was no better. The average number of doses of vaccine administered in the rheumatic fever series was almost two (1.8 per

utes, and is accompanied by a rapid rise in temperature. In two to three hours the temperature may have risen 2 to 5 degrees (Charts 1, 2 and 3). In a considerable number of cases there is a secondary rise in temperature, usually not so high as the primary, which may show

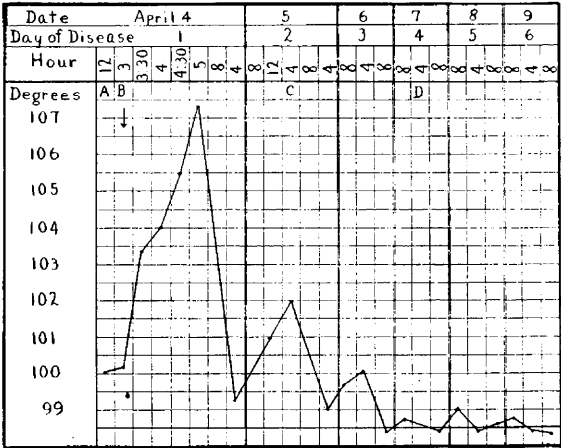


Chart 3.—Case 7. Rheumatic fever. Chart shows extreme rise of temperature following intravenous injection of typhoid vaccine. A, admission; B, 40 mg. typhoid vaccine intravenously; C, much better; D, no pain.

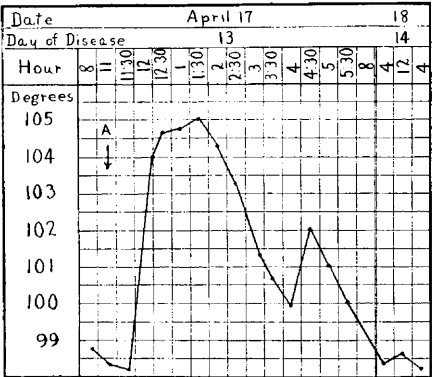


Chart 4.—Case 38. Gonococcus arthritis. Chart shows marked rise of temperature following intravenous injection of gonococcus vaccine. Reaction similar in all respects to typhoid vaccine reaction. A, 100 mg. gonococcus intravenously at 11:00.

itself in two to twelve hours (Charts 1 and 2). In some instances there is nausea and vomiting and quite a number of patients have a severe headache. In the course of the next three to six hours the temperature drops and by the following day it is usually normal.

Effect of Vaccine on Leukocyte Count.—Immediately after the injection of the vaccine, there is a slight fall in the leukocytes, followed in a short time by a rapid rise. In the course of two hours after the injection the leukocyte count may be four or five times the normal. For instance, in one case the count was 47,000, with 95 per cent. polynuclear neutrophils. The count rapidly returns to normal, though in Case 15 it was still 22,600 forty-eight hours after the injection. In five cases in which the leukocytes were counted one to two hours after the injection of vaccine the average count was 26,000.

Effect of Vaccine on Symptoms.—During the febrile period the patient nearly always feels better, and this relief from pain usually lasts twenty-four to forty-eight hours. The heat, redness and swelling may disappear entirely from the joints and complete and permanent recovery take place. More often there is a return of symptoms, which

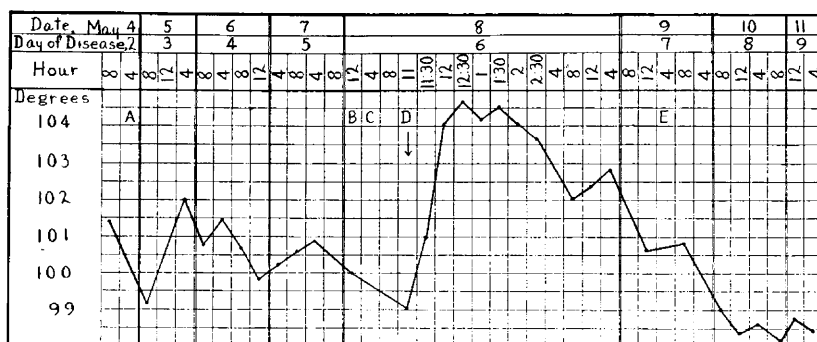


Chart 5.—Case 22. Pneumonia and empyema, followed by acute arthritis (rheumatic fever?); no relief from salicylates; immediate recovery after one intravenous injection of typhoid vaccine. A, sodium salicylate, 20 grains every four hours; B, no better; C, salicylates discontinued; D, 60 mg. typhoid vaccine intravenously at 11:00; E, pain and swelling gone; feels fine.

are usually not so severe as those before vaccination, and a second dose of vaccine may be necessary to bring permanent relief. On account, however, of the discomfort associated with these reactions to the vaccine, it seemed preferable in many of our cases to start the patients on salicylates, if one or two doses of the vaccine did not produce complete recovery. Twenty grains of salicylic acid or sodium salicylate, with 40 grains of sodium bicarbonate were given every two to four hours, depending on the severity of the symptoms, and continued until the patient was free from pain.

Contraindications.—In the present series we have considered severe cardiac or renal disease as contraindications to the use of intravenous vaccination. In markedly prostrated patients the vaccine is badly

borne, but may prove of much benefit. Such patients should be started with a small dose of 30 or 40 million bacteria.

Results.—Of the 33 cases of rheumatic fever and nonspecific arthritis studied, 13 (or about 40 per cent.) of the patients recovered completely in two to ten days without the aid of salicylates. (By recovery is meant the ability to be up and about the wards and free from pain.) The remaining 20 patients (or 60 per cent.) of the series received salicylates at some period during their attack. In 2 cases (Cases 22 and 33) the patients received salicylates without benefit for a number of days *before* the vaccine was tried. Of these 2 patients, 1 made a complete recovery after vaccination (Chart 5), and the other was much improved by it. The remaining 18 patients received vaccines first and salicylates afterward. Of these 18, three obtained no benefit from the vaccine; the remaining 15 improved, but were not completely cured until salicylates were given (Chart 6).

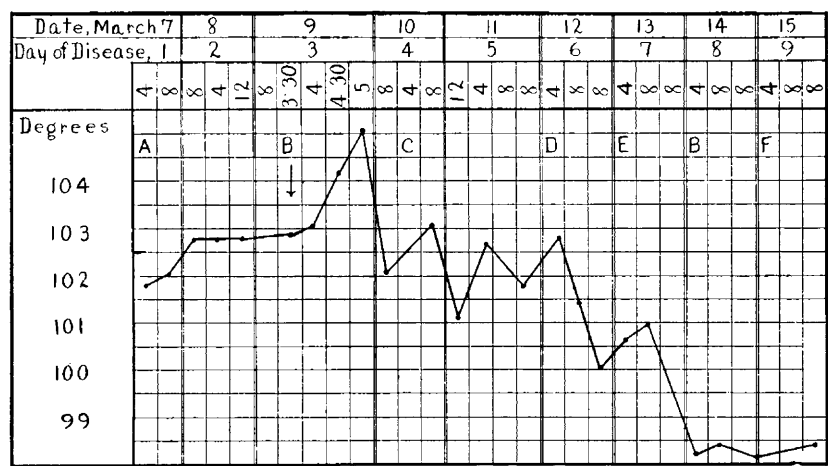


Chart 6.—Case 21. Rheumatic fever. Improved after vaccination, but relapsed. Rapid recovery after administration of salicylates. A, on admission; B, 40 mg. typhoid vaccine intravenously; C, better; D, relapse; E, salicylates started; F, better.

A noteworthy fact was that while the pain disappeared from the joints in many of these vaccinated patients, muscular pain persisted, particularly in the back or neck, and it was for these muscular pains that salicylates were resorted to.

The seven patients with gonococcus arthritis all made slow improvement during their stay in the hospital and appeared to be influenced little, if any, by the vaccine. Two of the patients received typhoid vaccines and the remainder gonococcus vaccine. There was no difference observed in the character of the reaction produced (Chart 4) or in the therapeutic value of the two vaccines. The gonococcus patients

CASES OF ACUTE ARTHRITIS—

| Case | Age | Sex* | Clinical Diagnosis | Complications | Previous illness | White Blood Cells |
|-----------|-----|------|--------------------|---|------------------------------|----------------------|
| 1. G. M. | 17 | ♀ | Rheumatic fever | Cervical adenitis; endocarditis | Rheumatic fever; tonsillitis | |
| 2. K. H. | 24 | ♀ | Rheumatic fever | Anemia | Measles; scarlet fever | |
| 3. M. C. | 14 | ♂ | Rheumatic fever | Tonsillitis; acute nephritis | Tonsillitis | |
| 4. M. D. | 24 | ♀ | Rheumatic fever | Endocarditis | Rheumatic fever | |
| 5. M. H. | 55 | ♀ | Acute arthritis | | Hemiplegia; angina pectoris? | |
| 6. G. G. | 21 | ♂ | Rheumatic fever | Tonsillitis; endocarditis | Rheumatic fever | 21,000 Polys. 69% |
| 7. M. M. | 42 | ♀ | Acute arthritis | Chronic tonsillitis; pyorrhea; endocarditis | Tonsillitis | |
| 8. Z. T. | 22 | ♂ | Rheumatic fever | Pharyngitis; pyorrhea | | |
| 9. G. C. | 27 | ♂ | Rheumatic fever | Tonsillitis | Rheumatic fever | |
| 10. M. R. | 40 | ♂ | Acute arthritis | Large tonsils; pyorrhea | Acute arthritis | |
| 11. W. K. | 34 | ♂ | Rheumatic fever | Tonsillitis; endocarditis | Gonorrhea 6 years ante | |
| 12. A. K. | 57 | ♂ | Rheumatic fever | Tonsillitis; endocarditis; pyorrhea | Tonsillitis; rheumatic fever | 7,000 |
| 13. B. S. | 46 | ♂ | Acute arthritis | Pyorrhea; bronchitis; delirium tremens | Gonorrhea 20 years ante | 16,800 Polys. 76% |

Cases in which Vaccine Was Supplemented by Salicylates

| | | | | | | |
|------------|----|---|-----------------|---------------------------------|---|----------------------|
| 14. P. B. | 24 | ♂ | Rheumatic fever | Furuncles; endocarditis | Frequent sore throat | 10,600 Polys. 70% |
| 15. J. F. | 40 | ♂ | Rheumatic fever | Sore throat | Rheumatic fever, 6 attacks | 22,600 Polys. 81% |
| 16. B. Sm. | 19 | ♀ | Rheumatic fever | Tonsillitis | Appendicitis; pneumonia; frequent sore throat | |
| 17. A. H. | 21 | ♂ | Rheumatic fever | Endocarditis; broncho-pneumonia | Rheumatic fever; frequent sore throat | 17,700 Polys. 82% |
| 18. | 26 | ♂ | Rheumatic fever | Endocarditis; coryza; pyorrhea | Rheumatic fever, 3 attacks | |
| 19. E. L. | 47 | ♂ | Acute arthritis | Vincent's angina | Gonorrhea 3 times; syphilis | |
| 20. M. P. | 37 | ♀ | Rheumatic fever | Pyorrhea | Rheumatic fever, 3 times | 14,000 Polys. 81% |
| 21. D. H. | 22 | ♀ | Rheumatic fever | Sore throat 1 week before | Measles | |
| 22. R. L. | 25 | ♂ | Acute arthritis | Lobar pneumonia; empyema | | 19,000 Polys. 87% |

* ♂ denotes male; ♀ female.

—TREATED WITH TYPHOID VACCINE

| Wassermann | Gonococcus Fixation | Number of Injections of Vaccine | Result | Remarks |
|------------|---------------------|---------------------------------|-------------------------------|---|
| Negative | Negative | 1, 50 million | Complete recovery in 48 hours | |
| | Negative | 1, 40 million | Complete recovery in 4 days | |
| | | 1, 30 million | Complete recovery in 5 days | Herpes labialis after vaccine |
| Negative | Negative | 1, 50 million | Complete recovery in 3 days | Herpes labialis |
| | | 2, 50 million each | Complete recovery in 5 days | Herpes labialis |
| Negative | Negative | 2, 40 million each | Complete recovery in 6 days | Blood culture sterile |
| | Negative | 1, 40 million | Complete recovery in 10 days | |
| Negative | Negative | 2, 50-60 million | Complete recovery in 10 days | Greek; history obtained with difficulty |
| Negative | Negative | 3, 40-60 million | Much improved (9 days) | Free from symptoms 24 hours after each injection, but relapsed twice |
| Negative | Negative | 1, 80 million | Complete recovery in 5 days | Uric acid in blood = 4 mg. per 100 c.c. |
| | | 1, 75 million | Complete recovery in 6 days | |
| Negative | Negative | 2, 60-70 million | Complete recovery in 6 days | |
| Negative | Negative | 1, 100 million | Complete recovery in 3 weeks | Delirium tremens appeared 2 hours after vaccination and lasted 4 days |

Cases in which Vaccine Was Supplemented by Salicylates

| | | | | |
|----------|----------|--------------------|--|---|
| Negative | Negative | 2, 50 million each | Improved after vaccine | Recovery under salicylates; blood culture sterile |
| | Negative | 1, 60 million | Much improved after vaccine | Relapse 3 days after vaccination; salicylates; recovery |
| | | 1, 70 million | Recovery in 2 days except for backache | Salicylates for backache |
| Negative | | 1, 40 million | No improvement | Blood culture sterile; on 4th day pneumonia; salicylates started; complete recovery |
| Negative | Negative | 4, 60-70 million | Improved temporarily after each dose | Blood culture sterile; two relapses; salicylates; recovery |
| Positive | Negative | 1, 50 million | Improved | Salicylates; complete recovery |
| | Negative | 1, 60 million | Much improved | Salicylates; complete recovery |
| | | 1, 40 million | Much better day after vaccination | Relapse; salicylates; complete recovery |
| | Negative | 1, 60 million | Complete recovery | Patient had received large doses of salicylates without benefit |

CASES OF ACUTE ARTHRITIS TREATED—

Cases in which Vaccine Was Supplemented by Salicylates

| Case | Age | Sex* | Clinical Diagnosis | Complications | Previous illness | White Blood Cells |
|-----------|-----|------|--------------------|--------------------------------------|---|----------------------|
| 23. P. H. | 46 | ♂ | Rheumatic fever | Endocarditis; pyorrhea | Gonorrhea, 20 years ante; rheumatic fever | |
| 24. F. S. | 26 | ♂ | Rheumatic fever | Endocarditis | Rheumatic fever; sore throats | 18,000 Polys. 87% |
| 25. J. O. | 22 | ♀ | Rheumatic fever | Tonsillitis; adenitis | Rheumatic fever; tonsillitis | |
| 26. J. M. | 13 | ♂ | Rheumatic fever | Endocarditis; pericarditis | | 12,800 Polys. 77% |
| 27. H. H. | 43 | ♂ | Acute arthritis | Sore throat 2 weeks before admission | Gonorrhea denied | |
| 28. J. R. | 28 | ♂ | Rheumatic fever | Coryza; endocarditis | Rheumatic fever; gonorrhea at 16 | |
| 29. P. C. | 32 | ♂ | Rheumatic fever | Endocarditis; paroxysmal tachycardia | Rheumatic fever; sore throats | 7,200 Polys. 82% |
| 30. G. A. | 22 | ♂ | Rheumatic fever | Sore throat; endocarditis | | |
| 31. M. Y. | 24 | ♂ | Rheumatic fever | Sore throat | Frequent sore throat | |
| 32. N. P. | 22 | ♂ | Rheumatic fever | Tonsillitis; endocarditis | Rheumatic fever; tonsillitis | 11,800 Polys. 84% |
| 33. L. A. | 28 | ♂ | Rheumatic fever | Endocarditis | Gonorrhea 5 years ante | 20,200 Polys. 82% |

Gonococcus Arthritis Treated with Gonococcus and Typhoid Vaccine Intravenously

| | | | | | | |
|-----------|----|---|----------------------|----------------------------------|------------------------------|----------------------|
| 34. J. M. | 27 | ♂ | Gonococcus arthritis | Gonococcus urethritis | Several attacks of gonorrhea | 7,800 Polys. 57% |
| 35. J. B. | 19 | ♂ | Gonococcus arthritis | Gonococcus urethritis | Chorea; rheumatic fever | 10,800 Polys. 75% |
| 36. F. G. | 42 | ♂ | Gonococcus arthritis | Gonococcus urethritis and iritis | | |
| 37. A. S. | 28 | ♀ | Gonococcus arthritis | Gonococcus vaginitis | Rheumatism 2 years ante | |
| 38. C. E. | 21 | ♂ | Gonococcus arthritis | Gonococcus urethritis | Gonorrhea 2 times | 8,000 Polys. 85% |
| 39. R. F. | 37 | ♂ | Gonococcus arthritis | Gonococcus urethritis | Gonorrhea 2 times | |
| 40. J. V. | 21 | ♂ | Gonococcus arthritis | Gonococcus urethritis | | 13,600 Polys. 83% |

* ♂ denotes male; ♀ female.

—WITH TYPHOID VACCINE—(Continued)

Cases in which Vaccine Was Supplemented by Salicylates

| Wassermann | Gonococcus Fixation | Number of Injections of Vaccine | Result | Remarks |
|------------|---------------------|---------------------------------|---|--|
| Positive | Negative | 1, 60 million | Improved | Herpes labialis (severe); salicylates; recovery |
| Negative | Negative | 1, 500 million | No improvement | Salicylates; recovery |
| Positive | Negative | 2, 50-70 million | Almost complete recovery | Salicylates given during last 2 days in hospital for muscular pains |
| Negative | | 1, 30 million | Improved | Blood culture sterile; vaccine not repeated on account of heart; salicylates; recovery |
| | Negative | 3, 40 million each | Temporary relief from vaccine | Salicylates for 2 weeks; much improved |
| | Negative | 1, 75 million | No improvement | Salicylates; recovery |
| Negative | Negative | 2, 400 million each | Improved | Blood culture sterile; salicylates; recovery |
| Negative | Negative | 7, 20-60 million | Improved but relapsed | Blood culture sterile; salicylates; recovery |
| Negative | Negative | 2, 400 million each | Improved | Salicylates given for pain in back; recovery |
| | | 2, 40 million each | Recovery, but relapsed 2 days after discharge | Blood culture sterile; salicylates for relapse; recovery |
| Negative | Negative | 3, 20-40 million | Much improved | Blood culture sterile; salicylates for 9 days; no improvement; then vaccine |

Gonococcus Arthritis Treated with Gonococcus and Typhoid Vaccine Intravenously

| | | | | |
|-----------------------------------|-------------|--------------------------------|---------------|--|
| Negative | Negative | 4, 40-60 million (typh. vac.) | Much improved | In hospital 5 weeks; left with some stiffness in back; otherwise O.K. |
| Negative | Weakly pos. | 7, (3 typh. vac., 4 gon. vac.) | Improved | In hospital 2 months; when discharged, walked with limp and had fluid in both knees |
| Negative | Positive | 8, 30-175 million (typh. vac.) | Much improved | In hospital 6 weeks; still having occasional pain when discharged, but practically cured |
| Negative | Positive | 5, (2 typh. vac., 2 gon. vac.) | Improved | In hospital 7 weeks; when discharged ankle was still sore, but could walk on it |
| Negative | Negative | 5, 50-100 million (gon. vac.) | Much improved | Herpes labialis; in hospital 3 weeks; still limping when he left hospital |
| Negative | Positive | 4, 60-100 million (gon. vac.) | Improved | In hospital 3 weeks; left hospital on crutches; still lame 1 month later |
| Positive with cholesterin antigen | Positive | 5, 60-100 million (gon. vac.) | Improved | In hospital 5 weeks; still lame when he left hospital |

remained in the hospital from three to eight weeks. The average duration of their stay in the hospital was five and one-half weeks. They all left the hospital in about the same stage of improvement; that is, with one or two joints still stiff and somewhat painful on motion, but with no signs of active infection in them. The injection of vaccine seemed to give relief for twenty-four hours or more; then the pain in the joints would return to the previous state.

Other Effects of Vaccine.—No unpleasant effects were noted from the vaccines other than the chill and fever and the constitutional symptoms above described. Five of the patients developed herpes labialis, apparently as the result of the vaccine, and one alcoholic patient had delirium tremens, which developed on the day after the vaccine was given.

DISCUSSION

The reaction produced by the intravenous injection of typhoid or gonococcus vaccine is usually quite rigorous and not a particularly pleasant experience for the patient. The question which immediately comes up is whether the results obtained by the vaccine are sufficiently brilliant to justify the use of this rather heroic measure. While it is true that in 40 per cent. of our cases of rheumatic fever (including the cases of acute arthritis) the patient recovered without the use of salicylates, it must be remembered that rheumatic fever is usually a self-limited disease and that in many instances the patient would make a rapid recovery even if no medication were given. From my own experience with thirty-three patients treated by this method I feel that salicylic acid is still our best weapon against rheumatic fever, and that the intravenous injection of vaccine or of foreign proteins should be employed only after salicylates have been ineffective.

As for the seven gonococcus cases, the vaccine seemed to have no permanent effect and, so far as I could see, exercised no influence one way or the other on the course or outcome of the disease. Miller reports similar results with his gonococcus arthritis cases. These are always difficult cases to handle, and appear to run their course in spite of all local or constitutional treatment.

It is interesting to speculate as to what causes the benefit which many of these patients received from intravenous vaccination. A number of explanations have been given. The leukocytosis may be responsible for their recovery, as emphasized by Gay¹³ and his co-workers. It seems more probable, however, that the rise in temperature is a more important factor; certainly we never see improvement in these cases of arthritis unless there is an accompanying pyrexia. In a case of chronic arthritis, which is not included in the present study, I gave the patient

13. Gay, F., and Claypole, E.: *THE ARCHIVES INT. MED.*, 1914, **14**, 662.

several intravenous injections of an autogenous *Streptococcus viridans* vaccine. The injections were followed by a slight malaise and headache, but there was practically no rise in temperature, and the vaccine had no effect whatever on the course of the disease.

Jobling and Petersen¹⁴ have shown that the intravenous injection of bacteria, protein split products, trypsin and kaolin, is almost invariably followed by more or less marked mobilization of serum protease and esterase. There is also a distinct rise in the anti ferment titer of the serum following such injections. As Jobling¹² says, however, these serum changes are more or less temporary and do not explain the permanent recovery of patients treated by intravenous injections of vaccine and other proteins.

For the present we must admit that no thoroughly satisfactory explanation can be given of this interesting phenomenon. Practically speaking, we have at our disposal a rather heroic therapeutic measure, at times quite efficient, but likely to prove dangerous in the hands of inexperienced workers. For the present we should recommend its use only after salicylates and other well established methods of treating arthritis have failed.

CONCLUSIONS

In forty cases of acute arthritis the patients have been treated by intravenous injections of typhoid or gonococcus vaccine. Thirteen of these patients, or 32 per cent., made a rapid recovery without recourse to any other treatment. Of the remaining twenty-seven cases, all but two patients showed improvement while receiving the vaccine. Twenty out of the twenty-seven, however, received salicylates before complete recovery took place. In the seven cases of acute gonococcus arthritis all of the patients showed gradual improvement under vaccine, but it was impossible to say how much of a factor the vaccine was in these cases.

The reaction produced by the vaccine is usually severe, consisting of a chill, with rapid rise in temperature, headache, and often nausea and vomiting. During this reaction there is a well-marked leukocytosis. Both the temperature and the leukocytes usually return to normal in a few hours.

This method of treatment is undoubtedly efficient in many cases of acute arthritis; but it is unpleasant for the patient, and may be dangerous when administered to improperly selected patients.

For the present, its use is recommended only in carefully selected cases, after salicylates and other well established methods of treating arthritis have failed.

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14. Jobling, J. W., and Peterson, W.: Jour. Exper. Med., 1915, **22**, 590, 597, 603, 141.