Revisiting Castlio and Ferris-Swift’s Experiments on Direct Splenic Stimulation in Patients With Acute Infectious Disease

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**Background:** In 1934, Yale Castlio, DO, and Louise Ferris-Swift, DO, published the results of a within-subjects experiment on direct splenic stimulation in patients with acute infectious disease (N=100). Their results, which used rudimentary statistical analyses, are still cited as evidence that osteopathic manipulative treatment augments immunity.

**Objective:** To retest the validity of Castlio and Ferris-Swift’s conclusions by applying contemporary statistical methods to their raw data.

**Methods:** Castlio and Ferris-Swift’s original 1934 data were not normally distributed and sample sizes were small. Therefore, the authors of the present study reanalyzed the data using several nonparametric statistical methods: Wilcoxon signed rank, Friedman, and Kruskal-Wallis tests.

**Results:** Contemporary statistical analysis confirms a modest posttreatment increase in leukocytes, a decrease in erythrocytes, a decrease in the Arnet index, and an increase in reticulocytes after the application of direct splenic stimulation for patients diagnosed with acute infectious disease. Contemporary reanalysis also confirms statistically significant posttreatment changes in the immune function tests. Findings were less conclusive for the leukocyte differential cell counts and for the effect of varying the number of splenic compressions.

**Conclusions:** Analysis of Castlio and Ferris-Swift’s 1934 data using contemporary statistical methods supports many of their original conclusions. However, faults in study design common to that era limit the article’s applicability for modern researchers. Additional research on splenic pump techniques using contemporary study designs and statistical methods is recommended.


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The spleen is a unique organ, located in the upper left portion of the abdomen, below the diaphragm. Its red pulp functions as a filter for the blood while the white pulp plays a role in adaptive immunity. As the body’s largest filter of red blood cells, the spleen removes old, damaged erythrocytes from circulation and efficiently recycles iron. The spleen fights infection by removing blood-borne pathogens (eg, encapsulated bacteria) from circulation. The lymphoid tissues of the spleen promote the body’s adaptive immune response to specific pathogens. These functions make the spleen an important organ for antibacterial and antifungal immune reactivity. In fact, individuals who lack a spleen are more vulnerable to pneumococcal infection.

One hundred years ago, it was widely understood that the spleen played a role in filtering the blood and in host immunity. Early osteopathic physicians saw the spleen as a reservoir for antibodies and leukocytes that could be expelled into general circulation by alternatively compressing and relaxing the tissues surrounding that organ. In the 1930s, the research team of Yale Castlio, DO, and Louise Ferris-Swift, DO, termed this form of manual treatment direct splenic stimulation, publishing two landmark articles detailing their research. Today, the osteopathic manipulative technique Castlio and Ferris-Swift used is most commonly known as the splenic pump.

The first Castlio and Ferris-Swift article, published in 1932, reported the effects of splenic stimulation in healthy individuals. A second study, published in 1934, reported the effects of splenic stimulation in patients hospitalized for acute infectious disease. Their research is still commonly cited in the osteopathic medical literature as evidence that lymphatic pump-type techniques boost immunity.

However, Castlio and Ferris-Swift based their conclusions on rudimentary statistical analyses. Results were reported as a percent of cases that generally had either a net increase or decrease from baseline. Because their methods do not conform to modern standards, their conclusions are open to debate. Fortunately, Castlio and Ferris-Swift published complete tables of their raw data, allowing future researchers to conduct additional analyses.

Our reanalysis of their 1932 paper on splenic stimulation in 100 normal subjects found significant increases in leukocyte counts and opsonic index and a decrease in erythrocyte counts (Figure 1). However, bias may have influenced their results, since the mean increase in leukocyte counts was sig-
agglutinative power
A measure of the agglutination level of red blood cells in response to a foreign body.10 Yale Castlio, DO, and Louise Ferris-Swift, DO,5 used colon bacillus for the foreign body and made graduated dilutions of serum with a salt solution from 1/5 to 1/50. The highest dilution at which agglutination occurred was reported. Agglutination at higher dilutions (lower values) indicates an increase in the agglutinative power of the serum.

Arneth index
A measure that reflects the age of the neutrophils based on the number of lobes in the nuclei.10 Younger neutrophils typically have one or two lobes while older neutrophils have as many as five or more. Individuals with a larger percentage of neutrophils with few lobes are said to have a “left shift” while those with a higher percentage of multilobed neutrophils have a “right shift.” Castlio and Ferris-Swift5 measured the index “in an effort to determine whether the increased leukocytosis that commonly follows splenic stimulation is due merely to the emptying of the spleen or, in part, to the stimulation of white cell formation by that organ.”

bacteriolytic power
A measure of the amount of bacterial destruction by the body.10 Castlio and Ferris-Swift5 measured the number of bacterial colonies to grow out on a plate incubated with a subject’s serum. Plus 1, one to 10 colonies; plus 2, 10 to 20 colonies; plus 3, 20 to 40 colonies; and plus 4, more than 40 colonies. Thus, lower values indicate the increased bacteriolytic power of the serum.

phagocytic index
A measure of the average number of bacteria ingested by phagocytes after a specified period of incubation, usually incubated at 37°C.10 Castlio and Ferris-Swift6 used leukocytes from the subjects, incubated them in a suspension of living bacteria for 20 minutes, then counted the ingested bacteria in 50 neutrophilic leukocytes for each experiment.

opsonic index
A measure of the potency of serum to opsonize bacteria. It is a ratio of the average number of bacteria ingested per phagocyte cell in infected serum divided by the corresponding value for normal serum.10 Castlio and Ferris-Swift5 calculated the opsonic index by dividing the posttreatment phagocytic index by the baseline phagocytic index.

Methods
Castlio and Ferris-Swift’s 1934 Study
We reviewed the 1934 article for methodologic details. The study was conducted at Lakeside Hospital in Kansas City, Mo. Castlio was a faculty member at the Kansas City College of Osteopathy and Surgery and Ferris-Swift was an intern at Lakeside Hospital. The only patient demographic information provided was the infectious disease diagnosis of each subject (Appendix). A total of 100 subjects were enrolled in the study. Sequential numbers were assigned to each study subject on trial entry. Participants were then allocated to one of four treatment groups in sequential blocks of 25 (eg, group 1, subjects 1-25). Study protocols (ie, number of splenic compressions, laboratory tests, testing sequence) varied by group assignment as outlined in Figure 2.

Subjects lay supine with their knees flexed while splenic stimulation was done. Alternate bimanual compressions and relaxations were applied to the tissues in front of and behind the spleen at a rate of 20 times per minute. Compressions were slow and deliberate; relaxations were abrupt.5

Figure 1. Glossary of medical terms used in the 1930s by Yale Castlio, DO, and Louise Ferris-Swift, DO.3,5

Significantly greater in a subset of 23 cases where laboratory tests were conducted by an honorary fraternity, relative to the cases managed by the Castlio and Ferris-Swift research team.

As previously noted, Castlio and Ferris-Swift6 published a second paper in 1934 detailing their experiments on direct splenic stimulation in 100 subjects hospitalized for various acute infectious diseases. The study design was more structured, more immunologic tests were done, and all laboratory work appears to have been performed by Castlio and Ferris-Swift.

The present study applied contemporary statistical analyses to the raw data published in that 1934 paper.5 Our primary hypothesis was that modern statistical analysis would support Castlio and Ferris-Swift’s original conclusions by showing a statistically significant posttreatment rise in serum leukocytes, percentage of neutrophils, and mature neutrophils in circulation; an increase in the opsonic index; and an increase in the agglutinative power and the bacteriolytic power of the serum. Also, contemporary data analysis would confirm a posttreatment decrease in circulating erythrocytes and that 30 or 40 splenic compressions would be as effective as 100.
Results

Table 1 summarizes our analysis of the leukocyte count data. The change from baseline was statistically significant at 30 minutes posttreatment (ie, groups 1 and 4, n=50). For these subjects, the mean increase in leukocytes was 895 (2529) cell/mm³ (P = .002). Pooling observation times also produced several other statistically significant changes from baseline.

The mean baseline leukocyte count for all 100 subjects was 10,481 (3851) cells/mm³. Comparing the baseline to first posttreatment blood draw (observation 5 minutes through 30 minutes, n=100) resulted in a mean posttreatment leukocyte count of 11,276 (4233) cells/mm³, a mean increase of 794 (2711) cells/mm³ (P = .003).

Comparing baseline data to that of the second posttreatment blood draw (observation 30 minutes through 120 minutes, n=100) yielded a mean posttreatment leukocyte count of 10,985 (3679) cells/mm³ for a mean increase of 504 (2215) cells/mm³ (P = .01).

Table 2 summarizes the results of reanalysis of Castlio and Ferris-Swift’s Arneth index data. All four sets of observations showed a significant decrease in the index relative to baseline. A decrease in the index (ie, right shift) suggests an increase in the percentage of circulating mature leukocytes.

Table 3 summarizes the results of the leukocyte differential cell count analysis. Most of the changes from baseline for this measure are not statistically significant. However, there was a small but statistically significant decrease in the mean percentage of endothelials, eosinophils, and basophils for pooled data from 30 and 45 minutes after treatment.

Application of Contemporary Statistical Methods

Our retrospective review of previously published data was exempt from institutional review board approval at A.T. Still University-Kirksville (Mo) College of Osteopathic Medicine.

Graphical examination of Castlio and Ferris-Swift’s 1934 data reveal that, for some parameters, data were not normally distributed and some data values were outliers. These data characteristics, in combination with small sample sizes for some of the comparisons, necessitated the use of nonparametric statistical analyses for the present study.

Due to the within-subjects design of the original study, we opted to use Wilcoxon signed rank tests to determine whether there was a significant change from baseline in the leukocytes, Arneth index, leukocyte differential cell count, erythrocytes, reticulocytes, phagocytic index/opsonic index, serum agglutinative power, and serum bacteriolytic power. To further analyze these outcome measures, we used Friedman tests to evaluate the data for changes over time within groups based on the number of splenic compressions each group received.

The effect of varying the number of compressions was also analyzed using Kruskal-Wallis tests to compare the groups on the change from baseline levels.

In addition to analyzing data for changes from baseline for each of the seven posttreatment time intervals, we pooled data from selected time intervals to achieve greater statistical power.

All data are reported as mean (SD). A P value of less than .05 was considered statistically significant.
Table 1 summarizes the changes from baseline in erythrocyte counts. There was a statistically significant decrease in mean erythrocyte counts at 5 and 30 minutes posttreatment. Most of the pooled observation times showed a decrease in mean erythrocyte counts. The mean baseline erythrocyte count for all 100 subjects was 4,221,500 (859,218) cells/mm³. Comparing baseline data to the first posttreatment blood draw (observation 5 minutes through 30 minutes, n=100) revealed a mean posttreatment erythrocyte count of 4,048,040 (788,098) cells/mm³, a mean decrease of 173,460 (577,398) cells/mm³ (P=.003). Comparing baseline to the second posttreatment blood draw (observation 30 minutes through 120 minutes, n=100) found a mean posttreatment erythrocyte count of 4,048,240 (737,677) cells/mm³ for a mean decrease of 173,260 (654,641) cells/mm³ (P=.01).

Table 2 summarizes the reticulocyte count analysis. It shows a small but statistically significant increase in mean reticulocyte counts at all but one posttreatment interval (ie, 60 minutes posttreatment).

Table 6 summarizes our reanalysis of immunologic test results reported by Castlio and Ferris-Swift. All results from this analysis were statistically significant at the P<.05 level except for results on serum agglutinative power at 10 minutes posttreatment (group 2). For agglutinative power at 45 minutes posttreatment, our findings show that agglutination occurred at a higher mean dilution, suggesting that agglutinative power was enhanced. The findings for bacteriolytic power indicate that fewer bacterial colonies grew out after 24 hours posttreatment. This result suggests that bacteriolytic power was also enhanced.

Table 7 presents the results of Friedman tests. We used this test to evaluate changes over time within groups by the number
of splenic compressions. The table shows the groups; each group’s two posttreatment testing intervals; the number of compressions received; and the mean baseline, first, and second posttreatment laboratory results. Only leukocyte and reticulocyte counts for group 4, which received 100 compressions, had statistically significant changes from baseline. Group 4 erythrocyte counts were suggestive of a change over time (P = .054). The Kruskal-Wallis test, used to test for between-group differences, suggested a greater increase in reticulocyte counts for group 4’s 100 compressions, relative to group 3’s 60 compressions (P = .054).

A major limitation of the original study design is that laboratory testing times and the number of splenic compressions used in treatment vary independently. However, there is one instance at 30 minutes posttreatment when only the number of compressions varies, allowing for between-group comparisons without testing intervals serving as a confounding variable. Kruskal-Wallis tests found no statistically significant difference between group 1 (30 compressions) and group 4 (100 compressions) for either leukocyte or erythrocyte counts at 30 minutes posttreatment.

Comment
In Castlio and Ferris-Swift’s 1934 article, they found “[a]n increase in the actual leukocyte count in about 80 per cent of cases, averaging approximately 2200 cells.”5 This statement is somewhat misleading because it is not a true mean but represents the average increase—when an increase occurred. Deeper in their text, Castlio and Ferris-Swift report that “[t]he average decrease, when that took place, was 2409 cells per cubic millimeter.”5 The present reanalysis of Castlio and Ferris-Swift’s data shows there was a modest increase in the mean leukocyte count with a peak rise occurring at approximately 30 minutes posttreatment and with considerable individual variability.

Castlio and Ferris-Swift conclude that there was “[a]n
increase in the percentage of polymorphonuclear neutrophils in about 75 per cent of the cases. However, our analysis found little change in the cell count differentials. The present study did confirm a posttreatment decrease in the Arneth index, indicating an increase in the number of mature neutrophils in circulation. This finding supports Castlio and Ferris-Swift's interpretation that splenic stimulation mobilized existing leukocytes sequestered in the spleen.

Consistent with Castlio and Ferris-Swift's original conclusions, the present study determined that there was a posttreatment decrease in circulating erythrocytes. With only 25 paired observations, the effect was statistically significant at 5 minutes posttreatment, suggesting an immediate effect. This finding further supports Castlio and Ferris-Swift's speculation that splenic stimulation augments the mechanical removal of erythrocytes, especially the aged and effete, from circulation.

Our analysis confirmed a posttreatment rise in reticulocyte counts, also consistent with Castlio and Ferris-Swift's original conclusions. An increase in the phagocytic index, opsonic index, serum agglutinative power, and serum bacteriolytic power were also confirmed. The immunologic tests are among the most robust statistically. However their clinical significance remains to be established.

Castlio and Ferris-Swift concluded that 30 to 40 splenic compressions were just as effective as a larger number. Results from our within-group analysis found that 100 compressions demonstrated statistically significant changes compared to baseline for leukocyte and reticulocyte counts, while fewer compressions were not significantly different from baseline. The more rigorous between-group analysis did not find a clear advantage for using 100 compressions—though a trend toward statistical significance was found for reticulocyte counts. As mentioned earlier, a major limitation of the original study design is that both the number of compressions and posttreatment test times vary, introducing confounding variables. Analysis of the one instance when time was not a confounding variable.
variable revealed no between-group differences for 60 versus 100 compressions for leukocyte and erythrocyte counts. Unfortunately, no comparisons can be made for 30 or 40 compressions using Castlio and Ferris-Swift’s original data without introducing time as a confounding variable. Our analysis of the effect of the number of compressions is inconclusive due to limitations of the original study’s design.

Another weakness inherent to the original study’s design is that the investigators were probably not blinded to the blood draw times. Characteristic of the era, double-blinding was uncommon and was not mentioned in the 1934 article. Hind sight must therefore acknowledge that the study was subject to the potential for investigator bias during data interpretation. Manually counting cells in a field or interpreting agglutination titers involves some interpretive subjectivity.

In fact, our reanalysis11 of Castlio and Ferris-Swift’s 1932 article,3 which examined splenic stimulation in apparently healthy individuals, found evidence that interpretive bias may have influenced the study’s results. In that earlier study, as previously noted, posttreatment leukocyte counts rose much higher in cases managed by an honorary fraternity from an osteopathic medical school compared to those managed by the researchers themselves.11 This source of potential bias is less of a factor in the current reanalysis because all cases and laboratory studies appear to have been managed by Castlio and Ferris-Swift. Nevertheless, investigator bias remains a limitation of the 1934 study, especially because all the major changes reported reflect desirable outcomes.

The underlying mechanism of action that explains how the splenic pump technique might alter blood cell counts and affect immune function still needs to be determined. Castlio and Ferris-Swift ascribe leukocyte increases to contraction of the spleen. Erythrocyte decreases they explain as alterations in splenic circulation. The rise in reticulocyte counts is consistent with a physiologic response to the loss of circulating erythrocytes. Castlio and Ferris-Swift speculated that changes in the opsonic index, serum agglutinative power, and serum bacteriolytic power were “due to contraction of the spleen with expulsion of its contained antibodies” and “increased rate of antibody formation due to antigen stimulation and circulatory stimulation.”

In the early 1980’s, Measel12 conducted experiments testing immune response in healthy individuals using the thoracic pump technique. He found a greater immune response to several subserotypes of pneumococcal polysaccharide in the treatment group relative to the control group.

A small study compared pectoral traction plus splenic pump techniques in 7 subjects and compared them to 5 control subjects.13 Thirty splenic compressions in 1 minute were used in the study protocol. There was a small posttreatment rise in serum basophils, but no significant change in any other complete blood count parameter. Interestingly, Castlio and Ferris-Swift found a small decrease in the combined percent of endothelials, eosinophils, and basophils for pooled data at

<table>
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<th>Table 6</th>
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<td>Baseline and Posttreatment Immunologic Tests Using Wilcoxon Signed Rank Tests (N=100)</td>
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<table>
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<tr>
<th>Posttreatment Time, min</th>
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<th>Phagocytic Index, Mean (SD)</th>
<th>Opsonic Index, Mean (SD)</th>
<th>Agglutinative Power, Mean (SD)†</th>
<th>Bacteriolytic Power, Mean (SD)‡</th>
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<td>4.36 (2.78)</td>
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<td><strong>30</strong></td>
<td>25</td>
<td>4.36 (2.78)</td>
<td>1.45 (0.57)</td>
<td>0.04 (0.02)</td>
<td>6.00 (3.51)</td>
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<td><strong>P</strong> Value</td>
<td><strong>&lt;.001</strong>*</td>
<td><strong>&lt;.001</strong>*</td>
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<td><strong>&lt;.001</strong>*</td>
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</table>

* Statistically significant change from baseline to posttreatment (P < .05).
† The highest mean dilution at which agglutination occurs with graduated dilutions from 0.2 to 0.02. Agglutinative power data at 10 and 45 minutes posttreatment was available for 23 subjects only. Laboratory work failed to provide results for 2 subjects.
‡ As noted in Figure 1, lower values indicate increased bacteriolytic power of the serum (eg, plus 1, one to 10 colonies; plus 2, 10 to 20 colonies).
30 and 45 minutes posttreatment.

Jackson and coauthors investigated lymphatic techniques and immune response to the hepatitis B vaccine in 39 healthy subjects. In that study, they found a faster rise in antibody titers relative to the control group. However, by the end of the study period, both groups had similar levels of antibody titers.

Three studies have failed to show improved influenza vaccine antibody titers after the use of lymphatic pump techniques. One of these studies, however, made use of the splenic pump technique and found a reduction in antibiotic use for nursing home residents during the influenza season.

In recent years, several animal studies have also provided evidence that lymphatic pump techniques augment the circulation of lymphatic fluid. Dery and coinvestigators showed that massage applied to the ventral thorax improved lymph uptake from the hind limb of rats. Knott and coauthors showed thoracic and abdominal pump techniques improved thoracic lymphatic duct flow in canine subjects at a rate that was similar to that of exercise.

Conclusion

Contemporary statistical analysis of Castlio and Ferris-Swift’s raw data from the 1930s on direct splenic stimulation in patients hospitalized for acute infectious disease supports many of their original conclusions. There is evidence that splenic stimulation causes a posttreatment rise in serum leukocyte counts, a decrease in erythrocyte counts, and stimulates the immune system. However, issues related to Castlio and Ferris-Swift’s original study design limit the conclusions that can be drawn. Nevertheless, their original work is remarkable as an early attempt to place the osteopathic medical profession on a firm scientific foundation. More work using contemporary study designs and techniques is necessary to further this line of inquiry.

References


### Appendix

Case number and acute infectious disease diagnosis for each subject who participated in the 1934 within-subjects experiment on splenic pump technique (N=100) conducted by Yale Castlio, DO, and Louise Ferris-Swift, DO. Clinicians will readily note that the diagnoses represented in this list are very different from the types of infectious disease that require hospitalization today. A few of these diagnoses are rare today (eg, tularemia). Others are no longer considered infectious disease (eg, rheumatoid arthritis). Adapted with permission from Kansas City (Mo) University of Medicine and Biosciences College of Osteopathic Medicine.

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<th>Subject No.</th>
<th>Group 1</th>
<th>Diagnosis</th>
<th>Subject No.</th>
<th>Group 2</th>
<th>Diagnosis</th>
<th>Subject No.</th>
<th>Group 3</th>
<th>Diagnosis</th>
<th>Subject No.</th>
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<td>100</td>
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