TABLE I.
Phosphorus Values in Human Heart Muscle.
Mg. per 100 gm. Fresh Muscle.

		Total P Mean ± PE	σ*	Acid-soluble P Mean ± PE	σ*	Residual P Mean ± PE	σ*
No Failure	36	180.3 ± 0.90	8.0	88.8 ± 0.99	8.4	91.0 ± 1.04	9.3
Failure	33	161.4 ± 1.15	9.8	72.3 ± 0.96	8.2	89.0 ± .91	7.7
Difference		18.9 ± 1.46		16.5 ± 1.38		2.0 ± 1.38	

*of the whole series.

The attempts to fractionate the acid-soluble fraction were unsuccessful. As might be anticipated, these labile compounds had hydrolyzed before we obtained the muscle; the estimation of the changes in this group must await the experimental production of heart failure. In a few instances, traces of soluble barium salts were obtained (phosphocreatine or hexosephosphate), but these were too small to measure. No pyrophosphate could be identified.[12] The orthophosphate was consistently 5 to 15 mg. % lower than the total acid-soluble phosphorus; this difference possibly is a measure of a portion of the nucleotid phosphorus which is either difficult to hydrolyze or is as yet unidentified.

Summary. The decrease in total myocardial phosphorus which accompanies heart failure is due to a decrease in the acid-soluble phosphorus compounds.

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Use of Mice for Testing Toxicity of Rabbit Therapeutic Antipneumococcic Serum.

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Since the newly developed *rabbit* therapeutic (unconcentrated) antipneumococcic sera, now being used with favorable clinical results,[1, 2, 3] even after processing of the raw serum by heating at 56°C.

[12] Lohmann, K., *Biochem. Z.*, 1928, **202**, 466.

[1] Horsfall, F. L., Jr., Goodner, K., and MacLeod, C. M., *Science*, 1937, **84**, 579.

[2] Horsfall, F. L., Jr., Goodner, K., MacLeod, C. M., and Harris, A. H., 2nd, *J. Am. Med. Assn.*, 1937, **108**, 1463.

[3] Horsfall, F. L., Jr., Goodner, K., and MacLeod, C. M., *N. Y. State J. Med.*, 1938, **38**, 246.

and absorption with kaolin,[4] have been found to cause chills in a considerable proportion of patients, the importance of testing each lot of rabbit antiserum for its chill-producing quality before injection into man has been emphasized.[3, 4] It is recommended that each of 3 *rabbits* be inoculated intravenously with 2.0 cc. of the processed rabbit antiserum and that their rectal temperatures be determined before, and one hour after, the injections. If the mean thermal elevation exceeds 1.3°F. it is said that the serum will produce chills in patients, whereas lots of serum "negative in rabbits" will not do so.[3, 4]

It occurred to us that a toxicity-test utilizing a different species of animal than that from which the antiserum is derived, and not dependent entirely upon slight changes in rectal temperatures, would probably prove more satisfactory, and since the necessary technic for intravenous injection was familiar,[5, 6] we have investigated the possibility of using *mice* as test-animals.

Five rabbits, 3 of which had been immunized to egg-white and 2 to typhoid bacilli, were bled aseptically; the toxicity of these sera, before and after processing by Goodner's method,[4] was tested by intravenous injections of mice and rabbits whose rectal temperatures were taken 15, 30, and 60 minutes after injection, and when indicated, at 90- and 120-minute intervals.

Preliminary trials showed that the raw rabbit serum from *each* of the 5 rabbits was equally toxic for mice and that 1.0 cc. was close to the minimal lethal dose when given *intravenously*.

TABLE I.
Toxicity of Raw and Processed* Rabbit Serum for Mice and Rabbits.

Test animals	No. inoculated	Inoculum: Rabbit serum	Inoculum: Dose, cc.	Symptoms	Aver. max. temp. change °F	Died
Rabbits	6	Raw	2.0	None	+0.2	0
"	14	Processed	2.0	"	+1.0	0
Mice	14	Raw	1.0	Severe, prolonged	>—4.4†	11
"	9	Processed	1.0	Slight and transient,	+1.2	0
"	8	"	1.5	or none	—2.5	0

*Sera processed as follows: (1) heated at exactly 56°C for 30 minutes, (2) mixed with sterile kaolin and refrigerated overnight, (3) centrifuged to remove kaolin, (4) heated again for one-half hour at 56°C.

†Ten animals only.

[4] Goodner, K., Horsfall, F. L., Jr., and Dubos, R. J., *J. Immunol.*, 1937, **33**, 279.

[5] Burdon, K. L., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 340.

[6] Burdon, K. L., *J. Lab. and Clin. Med.*, in press.

The results of our comparative tests of the same sera in mice and in rabbits are summarized in Table I.

These experiments demonstrated the great reactivity of mice toward the toxic qualities of rabbit serum, and indicated that toxicity of this serum may be regularly and easily demonstrated in mice in an unmistakable manner. The mice appeared to be definitely superior to rabbits as test animals since their reactions to toxic rabbit sera were more uniform and far more determinate.

Contrary to a general impression, no real difficulty was presented by the necessity of making intravenous injections in the test mice, for, with the use of a suitable holder,[6] these inoculations may be made rapidly and accurately by a single worker.

The fact that the elements in rabbit sera toxic for mice were removed by a method which Goodner has found effective in reducing chill reactions in man, makes it probable that a serum, so processed, causing no reaction in mice, would also be non-toxic for human beings.

Unfortunately we are unable to report at this time complete tests of this hypothesis because samples of the unconcentrated therapeutic antipneumococcic rabbit sera, now undergoing clinical tests by Horsfall, Goodner, and their collaborators, of known chill-producing potentialities in man, have not as yet been furnished us.

The usefulness of mice for toxicity tests is at present being investigated further with samples of the concentrated therapeutic antipneumococcic rabbit sera now being developed by the Lederle Laboratories.

Conclusion. The intravenous injection of mice may prove to be a more satisfactory procedure than the methods now in use for testing the potential toxicity of rabbit antisera intended for human therapy.