

The Influence of Polyvinyl Chloride (P. V. C.) Tubing on the Isolated Perfused Rat's Heart

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Perfusion of the isolated rat's heart through certain types of polyvinyl chloride tubing results in a deterioration of cardiac performance. Since plastics are commonly used in heart-lung machines and transfusion-sets, this observation may be of some importance.

THE isolated heart of the rat perfused by the Langendorff technic¹ can be kept beating for many hours. Over a period of several years we have performed hundreds of such experiments without difficulties.

In 20 consecutive perfused heart experiments, the electrocardiograms and inductocardiograms² of the isolated heart were found unchanged for periods of 4 hours or more. Subsequent expansion of our laboratory facilities made it necessary to rebuild our perfusion apparatus. After this, over 50 successive perfusions proved to be unsuccessful. Premature cardiac arrest and ventricular fibrillation occurred. Calcium, epinephrine, strophanthin and aminophylline, added to the perfusion fluid, were ineffective in combating the deterioration. A thorough investigation of the perfusion fluid did not reveal any change in chemical composition. Perfusion pressure was constant throughout all experiments. It seemed possible, therefore, that the polyvinyl chloride tubing which had been used instead of the glass tubing in the original set-up could be the responsible factor.⁴⁻⁶

Experiments were therefore designed to test this possibility.

Methods

White rats weighing about 250 Gm. were used for the experiments. The perfusion apparatus is depicted in figure 1. After the insertion of a

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cannula (*C*, fig. 1) in the aorta of the anesthetized and heparinized animal, the heart was removed and connected to the perfusion apparatus. The perfusion fluid was matched as closely as possible to the composition of the extracellular fluid of the rat.^{3, 7, 8} The perfusion fluid was saturated with 5 per cent CO₂ in oxygen (*A*, fig. 1). The pH of the perfusion fluid was 7.35. Gas bubbles were evacuated by bubble traps (*B*, fig. 1).

The perfusion fluid reached the heart by 2 identical circuits, one including a bottle of 750 ml. containing 500 ml. glass pearls, the other an identical bottle containing 50 ml. of P. V. C. slices with a thickness of 2 to 4 mm. and a diameter of 8 to 12 mm. Before every experiment the P. V. C. slices and the glass pearls were rinsed with distilled water. Perfusion pressure was regulated by altering the height of perfusion fluid containers.

Every experiment was started by perfusing the heart via the glass circuit for 10 to 20 min. Simultaneously the perfusion fluid was allowed to pass through the P. V. C. circuit. The perfusion velocity in both circuits was about 20 ml./min. The fluid soaked about 15 min. through the P.V.C. before it reached the heart. This was estimated with the use of methylene blue. By means of the stopcock (*K*, fig. 1), perfusion of the heart through glass or plastic was alternated. The glass spirals (*S*, fig. 1) were used to maintain the perfusion fluid at the desired temperature of 38° C.

The mechanical activity of the heart was recorded by means of a small Ticonal magnet (*M*, fig. 1) attached to the apex of the heart (*H*, fig. 1) and placed in the core of a coil. Cardiac contraction caused the magnet to move up and down. The resulting potentials in the coil induced by the movements of the magnet were amplified and recorded by an ordinary direct-writing electrocardiograph. The record was called "inductocardiogram."²

Results and Discussion

The passage of perfusing fluid through the polyvinyl chloride tubing resulted in a de-

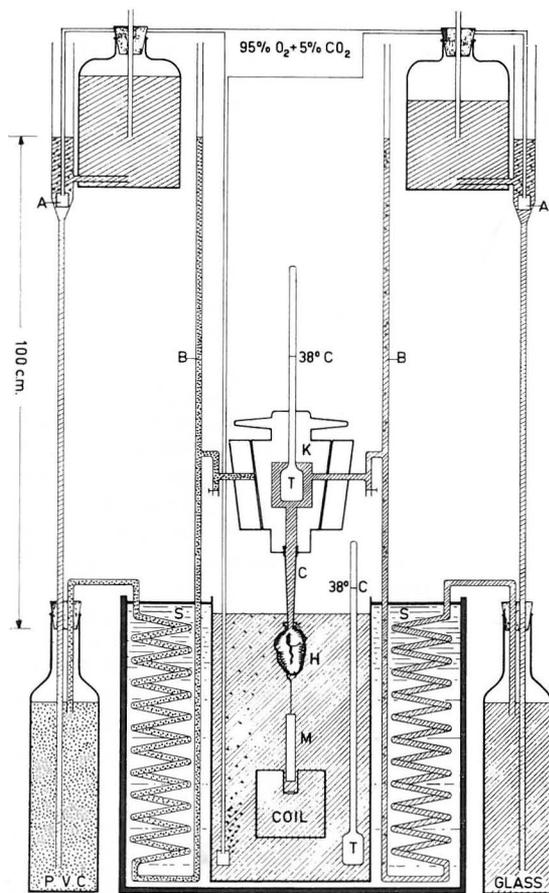


Figure 1

Diagrammatic representation of the set-up used to investigate the influence of polyvinyl chloride on the mechanical activity of the isolated perfused rat's heart. For details see text.

terioration of the heart contractions within 10 min. (A, table 1). Figure 2 shows the inductocardiogram of a heart perfused in succession via the glass and the P.V.C. circuit.

During P.V.C. perfusion the contractions of the heart diminished considerably and became irregular. After restoring glass perfusion, the mechanical activity increased but did not attain the previous level.

Perfusion with fluid from the P.V.C. reservoir (A, table 1) caused a progressive deterioration of contraction. Resumption of perfusion with fluid from the glass container did not restore the mechanical activity of the heart. The effects of P.V.C. perfusion were additive.

Table 1

Kind of P.V.C. Investigated:	A	B	C	D	E	Total
Number of hearts:	7	2	2	2	4	17
Number of investigations:	14	4	4	4	6	
Cardiotoxic effect: positive within 15 min.	14	0	0	3	5	

A total of 17 hearts was used to investigate 5 different types of polyvinyl chloride tubing and the results are summarized in table 1.

Chemical analysis of sample A (which is strongly toxic to the heart) and of sample B (non-toxic) revealed the following:

P.V.C. brand: A. Plastic: Polyvinyl chloride; Plasticizer: Content—43.7 per cent. The plasticizer concerned is an ester of phthalic acid, probably di-2 ethylhexyl-phthalate; Stabilizer: An organic tin compound. The organic part of the molecule is unknown. About 1 per cent of this stabilizer was used.

P.V.C. brand: B. Plastic: Polyvinyl chloride. Plasticizer: Content—34.5 per cent. An ester of phthalic acid, probably di-2 ethylhexylphthalate. Stabilizer: A barium-cadmium stabilizer, with an excess of barium. This means that a mixture of barium and cadmium salts of fatty acids was used for stabilization.

From the above data the following conclusions were drawn: The polymer proper (polyvinyl chloride) common to both samples is not responsible for the cardiotoxic effect because only sample A is deleterious to the heart. The plasticizer does not cause the effect either. It should be noted that in case the plasticizer were the cause, it would rapidly be extracted by the salt solution from the more elastic tube with the higher content of plasticizer, and much more slowly from the hard tube with the lower plasticizer content. In the latter case, i.e. if the plasticizer were the cause, the effect would also be observed at the harder tube in a retarded way. As this was not observed, the plasticizer cannot be the cause either.

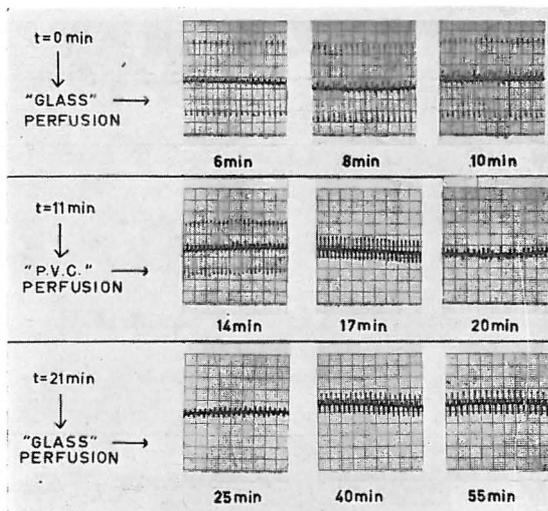


Figure 2

The inductocardiogram of an isolated rat's heart, perfused successively via the glass circuit, the polyvinyl chloride circuit and the glass circuit again. Paper speed 10 mm./sec.

The remaining possible cause is the stabilizer. It appears that the barium-cadmium stabilizer has no disturbing effect, whereas the organic tin compound has. Furthermore the extractability of the compounds in question with a salt solution can play an important role. It is possible that both materials may be toxic but only the latter can be extracted by the perfusate.

If in both cases one added chemical would be concerned, the extractability is larger in the soft elastic product. It is possible that traces of an emulgator likewise play a part in the process. Further tests are necessary in order to obtain better understanding of the mechanism that is responsible for cardiac depression.

Summary

Some brands of polyvinyl chlorides interfere with cardiac contraction, whereas other brands do not. Chemical investigation showed that the stabilizer is most probably responsible for the cardiotoxic effect. It is suggested that

all types of polyvinyl chloride used for medical and biological applications should be tested with this technic.

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Summario in Interlingua

Certe typos de chloruro polyvinylic interfere le contraction cardiac durante que alteres ha nulle tal effecto. Un investigation chimic provava con alte grados de probabilitate que le stabilisator es responsabile pro le effecto cardiotoxic. Es proponite que omne typos de chloruro polyvinylic usate in applicationes medical e biologic deberea esser testate per le technica hic describite.

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