INTRODUCTION

The effects on blood vessels of drugs commonly used in anaesthesia are of great interest to the clinician whose constant aim is to produce minimal physiological side effects during anaesthesia. A previous investigation using the Sandison Clark "regenerated" type chamber on the rabbit ear has been reported (Seldon et al., 1942). The present research has been carried out with the "preformed" ear chamber and in some cases the results differ from this earlier report.

In the preformed chamber the blood vessels under observation are the original subcutaneous vessels of the rabbit ear; in the regenerated type the blood vessels are the vessels formed in the process of repair.

It would appear more satisfactory to assess the effects of anaesthetic agents on the normally innervated vessels of the animal and not in those of the repair blastoma.

EAR CHAMBER DESIGN

The ear chamber used is of the conventional Sandison Clark type (Clark et al., 1930), with a raised table 6 mm in diameter, 1.5 mm high. However, it differs in that the tissue depth (200 μ in preformed chambers) is adjusted by the height of the outer pillars, and that the entire chamber is constructed from perspex, including the "cover glass". The use of a thick cover glass, makes the whole chamber very rigid, and yet provides adequate clearance for microscope objectives over the range of magnifications employed.

EAR CHAMBER INSERTION AND SUBSEQUENT EXAMINATION

The animals used are semi-lopeared adult rabbits, 2-4 kg in weight. The animals are housed in separate cages, in an environmental temperature of 70°F (±2°F) and fed on a standard diet (Bruce and Parkes No. 18).

Preformed ear chambers are inserted in each ear, using a sterile technique. At operation after reflection of the skin flaps, the central disc of cartilage is dissected away, leaving behind the outer perichondrum and overlying blood vessels, nerves and lymphatics. The ear chamber is inserted, the central table fitting the hole in the cartilage, and the other components are
assembled and fixed into position. After operation, the animal is left for at least two weeks to allow for a completion of the demolition phase following injury, and a stabilization of the vascular bed. At the end of this period, the animal is trained to become accustomed to microscopic examination in the conscious state, using a rabbit holder which accommodates the animal in a sitting posture.

The animal is then ready for trials with pharmacological agents.

All experiments are carried out at constant room temperature (70°F) and constant conditions of illumination. Where possible the same chamber is used for multiple trials with different anaesthetics and drugs, allowing a suitable time interval for adequate recovery from each agent. This provides a uniformity of material, which minimizes idiosyncrasy and individual variation in behaviour, and also helps accustom the animal to anaesthetic procedures. The results recorded and illustrated in this paper are representative of the invariable effect produced by drugs. In occasional instances where it is considered that certain reactions are not due to the agent tested, but to complicating experimental factors (e.g. anoxia, nervous excitability), this is stated in the text.

The microscopic examination of the ear vessels is made on a “Holophot” photomicrographic unit, in which the ordinary quarter-plate camera is replaced with a 35-mm “Exacta” camera, enabling rapid repeated exposures, to record calibre changes in the vessels under observation. A vascular field is selected which contains a larger branching artery, and the changes in this vessel and the surrounding field are observed throughout a given trial. Whenever possible the same field is used for successive trials with various agents. After the ear chamber has been fixed to a specially designed stage applicator the animal is left to settle down, and several trial control exposures are made to record the “initial” tone or calibre of the vessels before proceeding to anaesthesia.

No attempt has been made to present the results quantitatively by measuring the size of the vessels. It is considered that this method is subject to an experimental error too large to permit quantitative assessment by measurement, of minute changes in vascular calibre which cannot be detected by ordinary visual examination of photographic records. Throughout an experiment, careful observations are made on the rate of blood flow in vessels, evidence of pulsation and the degree of vasomotion in arteries. In most experiments the changes in vascularity were also followed by simultaneous recording by a photo-electrical method from the opposite ear.

INTERPRETATION OF VASCULAR CALIBRE CHANGES IN EAR CHAMBERS

The Sandison Clark type ear chamber used in the experiments under consideration is of rigid construction. The tissues under observation cannot readily alter in total volume, and this factor profoundly influences the interpretation of the changes in the capillary bed observed when the volume of the layer contractile vessels alters with the exhibition of pharmacological agents. Active arterial and arteriolar contraction, brought about by a vasoconstrictor (e.g. adrenaline), is invariably accompanied by a compensatory dilatation of non-contractile small vessels (capillar-
ties and venules), the total vascular volume remaining relatively constant at the outset, until such time as transfer of liquid takes place from intravascular to extravascular spaces. The paradoxical behaviour of "rigid" tissues in respect of vascular calibre and blood flow, has been determined by Wright (1937), from experimental studies on the cranial contents.

The assumption that capillaries in the mammal behave passively, and do not possess the power of active muscular contractility, is still sub judice, although most investigators agree with this hypothesis (Clark and Clark, 1943; Chambers and Zweifach, 1947; Folkow, 1955). The behaviour of capillaries in rigid ear chambers, in response to vasotropic substances, also lends support to this view. It is considered that the term "capillary tone" should be rejected in favour of "capillary calibre". The term "tone" implies the presence of a tissue component which is actively contractile, i.e. a muscular tissue.

It follows that the observed changes in calibre of capillaries, venules and veins, in rigid ear chambers, must be interpreted with due attention to passive mechanical factors—a limitation reflected in other studies (Wilson, 1936; Levinson and Essex, 1943). This consideration particularly applies to the "preformed tissue" type chamber in which a much higher proportion of the total tissue volume consists of actively contractile vessels (arteries). The effects demonstrated in ear chambers on larger arteries and muscular arterioles are valid, but the reported effects on "non-contractile" vessels (capillaries and venules) cannot be regarded as representing the changes produced in the body.

Observations on the calibre of individual vessels in ear chambers in rabbits clearly indicate that it is impossible to define a "basal level of tone" for contractile vessels in these animals. In a trained animal, observed under apparently basal conditions in respect to environmental temperature, nervous excitability, posture, and illumination, the calibre of individual vessels of all sizes shows enormous variation. It is considered that interpretation of changes in calibre of a selected vessel (artery, arteriole or capillary) with the exhibition of a vasotropic agent, is completely unreliable unless gross pharmacodynamic changes are induced. Also, attempted quantitation of results by isolated measurements of vascular calibre, implies an experimental accuracy which does not exist. For this reason, studies of sizeable segments of larger arteries and the adjacent tissues, in thick preformed ear chambers, using lower powers of magnification, are preferable, and considered to provide much more consistent and useful information.

The confidence, expressed by Seldon et al. (1942), in a sampling technique which selects a single individual vessel for the interpretation of calibre changes, is not shared by the writers. It is also considered that the flexibility in the range of tone of peripheral arteries and arterioles, both general and local, in an animal under basal experimental conditions, together with the phenomena of phasic changes in tone—"vasomotion" (Clark and Clark, 1943; Wilson, 1936, 1953; Bozler, 1941, 1942, 1948; Evans and Schild, 1953)—makes an accurate assessment of "initial tone" subject to considerable error, particularly in anaesthetic experiments of relatively long
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duration. In the experiments under consideration, the initial tone of vessels in a tissue field was assessed by observation and photography over a period prior to anaesthesia. All possible precautions were taken to ensure that the animal was trained for the experiment, and basal environmental conditions observed. Whilst the initial tone determined in this way was used as a yardstick for subsequent changes in calibre of vessels following anaesthesia, more confidence was placed in any changes in calibre which took place during the experiment as the plane of anaesthesia altered, or if relative anoxia or hypercarbia were induced. The conclusions at the end of this paper are based on an integration of all the observed changes, rather than on strict comparisons of vascular calibre before and after anaesthesia.

ILLUMINATION

Recent studies indicate that strong illumination causes a relaxation in the tone of vascular smooth muscle (Furchgott et al., 1955). The relaxation is enhanced by increasing the intensity of illumination and a loss of tone as high as 50 per cent may be induced. The peak range of the action spectrum responsible for this photodynamic effect in the rabbit is 365–370 m\textmu, disappearing below 340 m\textmu and above 450 m\textmu. The light source employed in the present experiments consists of a Pointolite lamp. The light is filtered with a Wratten green filter (58A, B2 Dark) in conjunction with a heat-resistant glass filter, giving a transmission spectrum of wavelength 480 m\textmu to 600 m\textmu, with the maximum transmission at 520 m\textmu. This filter absorbs light over the range at which the photodynamic effect is reported to occur, and should eliminate alterations in tone due to the source of illumination employed. This has been confirmed by repeated direct observation of the calibre of arteries and arterioles, using nonfiltered and filtered light in ear chamber studies; removal of the filter causes a short initial increase in tone, followed by prolonged relaxation, despite the elimination of heating effects by retaining a heat-absorbent filter in position.

ADMINISTRATION OF DRUGS

Gaseous agents were administered by Gaddum's apparatus in which the rabbit's nose and mouth are inserted through a hole in an elastic membrane into a container. Fresh gas is introduced and used gas is removed by separate tubes, entering the container. Each tube has a low resistance one-way valve.

Irritant gases produce breath-holding by the rabbit which results in hypercarbia. This was avoided as far as possible by a slow induction when using ether, chloroform and trichlorethylene.

In order to obtain a fairly complete saturation of the animal with the agent, anaesthesia was continued for \(\frac{1}{2}\) to \(\frac{3}{4}\) hour before observations of the vessels were recorded. During this interval any effects from breath-holding would have disappeared.

The depth of anaesthesia with inhalation agents was gauged by the type of respiration, intercostal paresis occurring in deeper planes. The rapidity of response of the corneal reflex was useful in determining the lighter planes, and voluntary movements when the rabbit's nose
was touched were employed to indicate the return of consciousness.

Gases were delivered by a standard anaesthetic apparatus. Volumes were measured by recently calibrated rotameters. Volatile agents were vapourized by an air current passing through a Boyle's bottle. A minimum flow of 2 litres per minute was maintained throughout to prevent accumulation of CO₂.

The marginal vein of the ear was employed for intravenous injections. The depth of anaesthesia with thiopentone was determined by the corneal reflex which persists until deep levels of hypnosis are obtained.

**EXPERIMENTS AND RESULTS**

(1) In order to assess the intensity of arterial constriction in a preliminary experiment an injection of 0.5 ml of 1:1 pitressin, that is 5 pressor units, was given. The artery emptied almost completely (fig. 1b) and the small vessels dilated as would be anticipated from the closed-space hypothesis (vide infra). The chamber which illustrates this experiment is the same as that illustrating the effects of N₂O, cyclopropane and ether (see figs. 2, 3, 4).

**A. Effects of Anaesthetics**

(2) Nitrous Oxide.

Nitrous oxide was given in 80 per cent concentration with oxygen but this was insufficient to anaesthetize the rabbit. The concentration was then raised to 95 per cent until voluntary movement had stopped, when it was reduced to 90 per cent.

During induction with 80 per cent N₂O and 20 per cent O₂ (fig. 2b) slight arteriolar dilation was observed, due probably to
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FIG. 3
(a) Control (Art.=artery).
(b) Cyclopropane 50%, O₂ 50%: arterial constriction.
(c) Air: 10 minutes later: persistent arterial constriction.

breath-holding with CO₂ accumulation. With high concentration the vasodilatation (fig. 2c) is presumably due to the anoxia (5 per cent O₂), for the vessel became constricted (fig. 2d) when 10 per cent O₂ was given. It can be noticed in this figure that small vessel dilatation accompanies arterial constriction in accordance with the rigid space hypothesis concerning ear chambers.

Four minutes later while breathing 10 per cent O₂ and 90 per cent N₂O the vessels returned to normal (compare figs. 1e and 1a). It is concluded that N₂O had no direct effect on the artery studied, in contradiction to the findings of Seldon et al. (1942) who reported vasoconstriction in arteries and capillaries. All changes observed could be explained by changes in the tension of O₂ and CO₂ in the circulating blood.

(3) Cyclopropane.

Cyclopropane was given in 50 per cent concentration with O₂ when arterial constriction was observed (fig. 3b) which persisted for more than ten minutes after the rabbit started breathing air again (fig. 3c). Vasodilatation of the small vessels once again accompanied constriction of the artery. Increased vasomotion was noticed.

These results agree with those of Seldon et al. (1942) although their interpretation of the mechanism of this capillary dilatation in a closed chamber is open to doubt.

(4) Ether.

Ether vapour was given. In light anaesthesia when the corneal reflex first disappeared arterial constriction occurred (fig. 4b). With increasing depth arterial dilatation was seen (fig. 4c), and finally,
(a) Control (Art.=artery).
(b) Atropine 0.2 mg: arterial constriction 15 seconds later.
(c) Three minutes after atropine: artery normal.
(d) Ether: deep anaesthesia: arterial dilatation.
(e) Ether: light anaesthesia: arterial constriction.
(f) Ether: deep anaesthesia: arterial dilatation.

with return of consciousness, arterial constriction re-appeared (fig. 4d).

(5) Ether and Atropine.
During the previous experiment a copious oral and bronchial secretion occurred, and it was decided to repeat it with a preliminary intravenous injection of atropine 0.2 mg, which produced a profound arterial constriction in fifteen seconds (fig. 5b), returning to normal in three minutes (fig. 5c). Ether was then given and arterial dilatation occurred when a deep plane was reached (fig. 5d). When anaesthesia was lightened, arterial constriction occurred (fig. 5e), and when it was deepened again arterial dilatation (fig. 5f) recurred.

When the animal was allowed to awake constriction occurred, followed by dilatation and finally a return to normal.

Seldon et al. (1942) reported only an arterial constriction which may have been due to a lighter plane of anaesthesia during the experiment.

(6) Chloroform.
Chloroform was given to a rabbit whose ear chamber included the central ear artery (fig. 6a). Progressive arterial constriction (figs. 6b, 6c) occurred during induction and compensatory dilatation of small vessels in accordance with the closed-space hypothesis is clearly seen, and vasomotion was marked (figs. 6d, 6e). With increasing depth vasodilatation recurred (fig. 6f) but was not comparable with the original state of tone (fig. 6a).

The animal was now allowed to recover when arterial constriction reappeared (fig. 6g). With the return of the corneal reflex arterial dilatation again appears (fig. 6h), being interrupted by a short period of anoxia due to an obstructed airway. The anoxia was accompanied by constriction (fig. 6j) and when relieved dilatation recurred and increased (fig. 6k) until voluntary movements occurred. These were accompanied by arterial constriction and vasomotion (figs. 6l, 6m).

It will be noted that the calibre of small vessels (capillaries and venules) bears an
inverse relationship to the size of the arteries. This once again illustrates the passive behaviour of these non-contractile vessels in a rigid space and emphasizes the fact that observations on ear chambers allow no conclusions to be drawn as to the effect of a pharmacodynamic agent on these minute vessels.

(7) Trichlorethylene.

Administration of trichlorethylene in air produced slight constriction in the arteries accompanied by dilatation of the veins and small vessels (fig. 7b). On withdrawing the anaesthetic arterial dilatation occurred (fig. 7c), and on awakening this was reversed and profound constriction

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**Fig. 6**

(a) Control: note large central ear artery (Art. = artery).
(b) Chloroform: very light anaesthesia: arterial constriction (note compensatory dilatation of small vessels).
(c) Chloroform: light anaesthesia: progressive arterial constriction.
(d, e) Chloroform: light anaesthesia: two phases of vasomotion.
(f) Chloroform: deep anaesthesia: arterial dilatation (note disappearance of small vessels).
(g) Chloroform: light anaesthesia: arterial constriction.
(h) Rabbit conscious: arterial dilatation.
(i) Conscious, anoxia: arterial constriction.
(k) Conscious oxygenated: arterial dilatation.
(l, m) Conscious: two phases of vasomotion.
(a) Control (Art. = artery).
(b) Trichlorethylene: light anaesthesia: arterial constriction (compare artery in lower right field).
(c) Air: still anaesthetized: arterial dilatation.
(d) Rabbit conscious: arterial constriction.

(fig. 7d) accompanied the reappearance of voluntary movements.

8) Thiopentone.
Thiopentone was injected intravenously in 0.5 per cent solution in divided doses of 5 mg/kg to avoid the fall in blood pressure which follows the rapid injection of an anaesthetic dose. After 20 mg/kg had been given the arteries were slightly dilated (fig. 8b). ββ methyl ethyl glutarimide (Megimide) was then given in 0.5 solution in a dose of 10 mg/kg. This produced a moderate arterial constriction and compensatory dilatation of the small vessels (fig. 8c).

Further administration of thiopentone in 5 mg/kg increments up to 15 mg/kg (making the total dose 35 mg/kg) reversed the arterial constriction and restored the picture to normal (figs. 8d, 8a).

Seldon et al. (1942) reported dilatation of both arteries and smaller vessels. We have found that, whilst arterial tone is decreased, the small noncontractile vessels in a rigid chamber do not dilate, but, on the contrary, passively collapse.

B. Effects of Relaxant Agents
It was decided to investigate the effects of relaxant drugs on the preparation. For this purpose paralysing doses were injected intravenously and artificial respiration by intermittent positive pressure employed, using a pump delivering 100 mg per stroke at a rate of 18 cycles per minute until voluntary respiration returned.
(9) d-Tubocurarine Chloride.

d-Tubocurarine (0.06 mg/kg) was given and a slight arterial dilatation occurred (fig. 9b).

When artificial respiration was discontinued and voluntary respirations were resumed a profound arterial constriction occurred (fig. 9c). This was presumably due to the rabbit becoming active (cf. vasoconstriction with recovery from anaesthesia (figs. 4d, 7d)) and the vessel again approached normal tone in two minutes (fig. 9d).

(10) Gallamine Triethiodide (Flaxedil).

0.15 mg/kg of gallamine triethiodide was given. This was followed in one minute by a slight transient arterial constriction (fig. 10b) which was relieved after a further minute, there being a slight dilatation (fig. 10c).
tion (fig. 10c). Application of a painful stimulus at this time by squeezing the ear produced constriction (fig. 10d).

Resumption of voluntary breathing had no effect on the artery (fig. 10c), but a painful stimulus now produced a more profound constriction than that during the period of paralysis (fig. 10f).

Marked vasomotion was noticed at the completion of the experiment and fig. 10g shows a wave of contraction passing along the artery.

(11) *Suxamethonium Chloride (Scoline)*

Suxamethonium chloride was given in a dose of 0.5 mg/kg. A profound arterial constriction followed two minutes later (fig. 11b) and subsequent dilatation was very gradual. Nine minutes after the injection, when normal respiration was established (fig. 11c), a residual moderate constriction was present.

(12) *Thiopentone and Suxamethonium.*

As it was thought that the constriction produced by suxamethonium may have been due to conscious influences, 20 mg/kg of thiopentone was given. This produced slight arterial constriction (fig. 12b) which was probably due to the fall in
blood pressure which follows the rapid administration of this agent. Suxamethonium 0.5 mg/kg was then given. A marked dilatation followed (fig. 12c) before artificial respiration was commenced, but one minute after the injection the vessel had returned to the same state (fig. 12d) as that following the thiopentone (fig. 12b).

With the return of consciousness a slight dilatation occurred (fig. 12e) but tone was still greater than in the control observation.

(13) Nerve Block of Ear and Suxamethonium.

In order to find whether suxamethonium had any direct effect on the artery, the nerves at the base of the ear were blocked by infiltration with 0.1 per cent lignocaine solution. Figure 13a shows relaxation of tone following the ear block.

Injection of suxamethonium 0.5 mg/kg then produced a profound constriction (fig. 13b) similar to that following its administration in the conscious rabbit (fig. 11b). Progressive dilatation followed until four minutes later (fig. 12c) the vessel reached its former state of dilatation.

(14) Hexamethonium.

2 mg hexamethonium/kg were given and a mild arterial dilatation followed (fig. 14b). A painful stimulus was applied and minimal constriction followed (fig. 14c) instead of the usual marked arterial change. One minute after the painful stimulus the artery was still dilated (fig. 14d).

DISCUSSION AND CONCLUSION

Ear chambers provide an ideal method for the direct visual observation of the effects of drugs on arteries and arterioles.
Also, changes in the systemic arterial pressure tend to produce variations in vascular tone. A fall in blood pressure to shock levels is invariably associated with marked vasoconstriction. Minor variations in arterial pressure are associated with variations in vascular tone, although it is difficult to determine which change is primary. Folkow (1949, 1952), from studies on reactive hyperaemia following temporary arterial occlusion in a limb, postulates that a fall in intravascular pressure, by reducing the stretching stimulus to the vascular smooth muscle, results in a decrease in tone—a conclusion supported by Hilton (1953), Patterson and Shepherd (1954) and Greenfield and Patterson (1954). The effect of this factor in our experiments is not known. Whilst the blood pressure can be readily recorded in the ear of the rabbit (Grant and Rothschild, 1934; Anderson, 1922) the pressure recorded at different sites on the central artery varies greatly with the size of the vessel proximately and a method of measuring the pressure in the length of vessel under observation in the chamber has not been developed.

For the inhalation anaesthetic agents tested, except N₂O, a light plane of anaesthesia invariably produced arterial constriction. This supports the current view that anaesthetics initially stimulate the vasomotor centre. In the case of ether and chloroform, a deep plane of anaesthesia was produced, and arterial dilatation ensued, presumably due to depression of the vasomotor centre. These changes are reversible by altering the plane of anaesthesia.

In the case of nitrous oxide anaesthesia, all changes in the vascular calibre ob-
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served can be explained in terms of changes in oxygenation and CO₂ retention. In our opinion the difficulty encountered in inducing a steady plane of anaesthesia with this anaesthetic agent in an unpremedicated rabbit, without hypoxia, invalidates any evidence that nitrous oxide has a direct pharmacological action on vascular smooth muscle.

Arterial constriction produced by cyclopropane (fig. 3b), as reported by Seldon et al. (1942), agrees with present clinical impressions that cyclopropane anaesthesia, without CO₂ retention, is not accompanied by increased arteriolar bleeding.

Return of consciousness and voluntary movements, following anaesthesia were invariably accompanied by a marked increase in vascular tone—always in excess of the initial tone prior to anaesthesia (see figs. 4d, 6l).

Thiopentone produced a diminished vascular tone, as reported by Seldon et al. (1942). It was found that β ethyl methyl glutarimide (Megimide), which has been reported as a barbiturate antagonist by Shaw et al. (1954), produced arterial constriction, reversed by additional doses of thiopentone (figs. 8c, 8d).

The investigation of relaxant drugs on vascular tone in the conscious animal presents great difficulties. These agents necessitate the use of artificial respiration, which has a complicating effect on vascular tone by causing nervous stress; and in the case of intermittent positive pressure respiration, as used, venous return is said to be impaired (Cournand et al., 1948). The results obtained suggest that d-tubocurarine which produces a diminution in vascular tone, depresses preganglionic sympathetic synapses without preliminary stimulation. This depression is not complete with a dose employed to produce respiratory paralysis, in that a subsequent painful stimulus produced intense constriction.

Gallamine triethiodide appeared to produce a preliminary stimulation before depression (figs. 10b, 10c). Again, block was incomplete as pain produced constriction (fig. 10d) but not comparable to that produced by a similar pain stimulus after paralysis had worn off (fig. 10f). Suxamethonium produced profound constriction in an artificially respired conscious animal (fig. 11b). When the drug was preceded by a hypnotic dose of thiopentone, and after respiration was artificially stabilized, the constriction was still present (fig. 11d). It is considered that this constriction produced by suxamethonium is not an artifact due to respiratory embarrassment or nervous excitation, suggesting there is either a direct effect on vascular smooth muscle or sympathetic ganglionic stimulation. The central effect was abolished by blocking the vasomotor nerves at the base of the ear, with consequent reduction in tone (fig. 13a). Suxamethonium still produced profound vascular constriction (fig. 13b) followed by gradual return to the initial dilated state (fig. 13c). This suggests that suxamethonium directly stimulates vascular smooth muscle.

Arterial dilation followed the exhibition of hexamethonium (fig. 14b) in accordance with its ganglion blocking properties (Paton and Zaimis, 1949). A subsequent painful stimulus produced a minimal change in calibre (fig. 14c) indicating a block, more complete than that apparently produced by curare and gallamine.
SUMMARY

(1) The effects of anaesthetics, relaxant agents and hexamethonium, on vascular smooth muscle have been studied by the preformed tissue Sandison Clark ear chamber technique in the rabbit.

(2) The limitations and interpretations of the behaviour of contractile and non-contractile vessels, in ear chambers, are discussed.

(3) The results obtained have been described, and interpreted with due attention to complicating factors such as oxygen lack, CO₂ excess, nervous stress and variations in systemic blood pressure.

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REFERENCES


EDITORIAL—continued

In his judgment, the Presiding Judge, Mr. G. Glynn Blackledge, Q.C., said that he was satisfied that the extravious injection of a small quantity of solution could happen without any negligence on the part of the operator. He held that Dr. I. P. C. had followed the correct technique and had stopped the injection as soon as he realized that the point of the needle was outside the vein. He found no evidence of negligence on the part of Dr. I. P. C. and accordingly gave judgment for the defendants with costs.

The importance of this judgment, with its implication, that "res ipsa loquitur" is not always proof of negligence, cannot be overemphasized.