THE INFLUENCE OF HYPOTENSIVE DRUGS ON RENAL
STRUCTURE IN EXPERIMENTAL HYPERTENSION,
(with particular reference to the relationship of
hydrallazine to the experimental reproduction of
disseminated lupus erythematosus).

VOLUME III

A thesis submitted for the degree of Doctor of
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ILLUSTRATIONS

The arrangement of the illustrations in a separate volume has been necessitated by technical reasons associated with their mounting.

The illustrations form a sequence corresponding to that of the experiments, and the captions provide sufficient data to allow them to be reviewed independently of the text.
Figure 1.

Normal rat kidney

Normal glomerulus of rat for comparison with subsequent illustrations.

Picro-Mallory. x 800.
**Figure 2.**

**Normal rat kidney**

Normal renal proximal convoluted tubules for comparison with later illustrations. Note the extremely small lumen and the position of the nuclei in the epithelial cells.

Haematoxylin and Eosin. x 1000.
Figure 3.

Normal rat kidney

Normal renal tubules for comparison with later illustrations. The brush border of the proximal convolutions is clearly shown, with the rudimentary lumina.

Picro-Mallory. x 1000.
Figure 4.

Normal rat kidney

The structure of the normal cortical collecting tubules is shown in this illustration. In the upper part of the figure a longitudinally divided collecting tubule is seen. Nearby are convoluted tubules; note the granular cytoplasm.

Haematoxylin and Eosin. x 1000.
Experimental Series I.

Figure 5.

Renal effects of Deoxycortone (D.C.A.)

This illustration and those subsequent to it show the evolution of the glomerular changes induced by the rapid absorption of excess D.C.A.

In the present illustration 2 enlarged glomeruli are seen. That on the right shows minimal swelling of the epithelial and endothelial cells of the tuft with an increase in the amount of intercellular material. The glomerulus on the left shows the appearance described as ballooning; it closely resembles that caused by the accumulation of fat in occasional forms of nephrosis. In the present instance swelling of these cells is believed to be the result of an osmotic electrolyte and water disturbance, and is analogous to the collecting tubular changes shown in later illustrations. Note the dilated tubules.

Picro-Mallory. x 500.
Figure 6.

**Renal effects of D.C.A.**

A glomerulus at a slightly later stage of development of the D.C.A. lesion. Several cells are now considerably distended and the tuft as a whole is large. Nearby is a dilated collecting tubule.

*Micro-Mallory. x 600.*
The cell changes are now more widespread and the greater part of the tuft is involved. It is often difficult to be certain whether the ballooned cells are epithelial or endothelial in origin. Many resemble epithelial cells, but distortion is often severe.

Picro-Mallory. x 600.
Figure 8.

Renal effects of D.C.A.

2 glomeruli are shown in this illustration. That on the right shows cellular ballooning.

That on the left has undergone more severe disorganisation. Its left lateral and upper part show hyaline droplet change and replacement fibrosis. The central part contains a small number of extremely dilated cells, while its lower and right lateral part is more normal. The nearby tubules show moderately severe epithelial cell changes of a type described later; many are dilated.

Micro-Mallory. x 500.
Figure 9.

Renal effects of D.C.A.

In this illustration an enlarged glomerulus similar to those seen in previous figures is shown, stained by the periodic acid-Schiff to demonstrate the increased amount of intercellular Schiff-positive material, the accumulation of which takes place under the action of excessive doses of D.C.A. The nearby tubules are only slightly altered - the brush border of the proximal convolutions is clearly shown.

P.A.S. x 550.
Figure 10.

Renal effects of D.C.A.

The cytological disturbance in this glomerulus is extreme. The tuft is large. Near the point at which the afferent arteriole enters the glomerulus there is a small accumulation of fibrinous hyaline material. A collecting tubule in the lower part of the figure is dilated while the proximal convolutions appear intact.

Picro-Mallory. x 600.
Renal effects of D.C.A.

This glomerulus shows extreme cellular dilatation and is now hardly recognisable. Around the tuft, and apparently involving its capsular epithelium, are aggregates of cells with dense round nuclei. Many of these cells are swollen although to a slighter degree than those of the tuft. The appearances are those often seen as a result of D.C.A. overdosage.

Nearby tubules contain proteinaceous material and are dilated.

Picro-Mallory. x 600.
Renal effects of D.C.A.

Gross glomerular enlargement characteristic of the uniformly widespread change seen in excessive D.C.A. overdosage. The great majority of the tuft cells are ballooned owing to a form of osmotic disturbance. Small aggregates of eosinophilic protein-containing material are seen among the tuft cells and in several places the tuft is in contact with the capsular epithelium. The latter has undergone proliferation.

Picro-Mallory. x 500.
Figure 13.

Renal changes due to D.C.A.

There is no fundamental difference between the structure of the enlarged glomerulus shown in this illustration and those shown in the previous two figures. When cellular ballooning and glomerular enlargement reach a certain critical stage the escape of protein into the subcapsular space occurs giving rise to the appearances seen in this figure. In the lower right corner similar protein-containing material lies within a collecting tubule. At the upper left corner a further tubule shows hyaline droplet change, an appearance frequently found in the tubules of nephrons showing severe damage.

Picro-Mallory. x 600.
Figure 14.

Renal changes due to D.C.A.

This glomerular tuft has undergone extensive distortion. The majority of its cells are dilated, and the tuft very greatly enlarged. Protein-containing fluid has escaped into the subcapsular space and lies scattered among the tuft cells. This illustration and the succeeding one should be compared with figure 56 of Experimental Series II, page 112.

Picro-Mallory. x 500.
Figure 15.

Renal changes due to D.C.A.

The cells of this glomerulus are less severely dilated than those of the previous illustration, but nevertheless much protein-containing fluid has escaped into the subcapsular space. The glomerular tuft is very much enlarged and scattered among its cells are small numbers of hyaline droplets. Proliferation of capsular connective tissue fibres has occurred, an appearance seen in the later stages of the evolution of these lesions. Protein also lies within the collecting tubule seen at the left margin.

Picro-Mallory. x 400.
Figure 16.

Renal changes due to D.C.A.

This is believed to represent a later phase in the evolution of the change, the initial stages of which are shown in the previous illustration. In the centre of the glomerular tuft distended, ballooned cells are seen. Around them connective tissue fibres are present in excess and they in turn are surrounded by numerous dilated endothelial-type cells which have spread to involve the nearby tubules. No fibrinoid is seen in this lesion; it should be compared with figure 20, where the early accumulation of central fibrinoid is seen.

Picro-Mallory. x 260.
Figure 17.

Renal changes due to D.C.A.

The appearance of this glomerulus closely resembles that seen in the previous one. It is now difficult to appreciate that this condition has evolved from disintegration of a glomerular tuft without comparison with earlier figures. The change is of a similar character to that seen around arterioles undergoing fibrinoid necrosis as a result of overdosage of D.C.A.

Micro-Mallory. x 340.
Figure 18.

**Renal changes due to D.C.A.**

The present illustration shows a focus of distended swollen cells lying about an apparently normal arteriole. The illustration shows the difficulty experienced in some instances in distinguishing perivascular from periglomerular reactions, and in some cases that distinction is probably not possible.

P.A.S. x 460.
Figure 19.

Renal changes due to D.C.A.

This figure shows distortion of a glomerular tuft caused by excess D.C.A. A gradual transition may be traced between the changes illustrated in the early stages of D.C.A. overdosage and those shown in the present illustration.

Part of a normal glomerular tuft is shown at the right lateral margin of the figure and serves to indicate the degree of enlargement of the central tuft.

Picro-Mallory. x 500.
Figure 20.

Renal lesions due to P.C.A.

The glomerulus illustrated in this figure is undergoing central fibrinoid necrosis. It is not certain whether this indicates central destruction of the tuft with collapse and the proliferation of swollen periglomerular cells, or whether, as is more probably the case, the whole of the cellular accumulation is in fact a swollen glomerulus. Notice the normal arteriole on the right passing towards the glomerulus.

Picro-Mallory. x 340.
Figure 21.

Renal lesions due to D.C.A.

The changes shown in the present illustration closely resemble those seen in the previous figure. On the right a normal arteriole may be traced passing towards a focus of fibrinoid necrosis which itself lies intermingled with swollen disintegrating ballooned glomerular cells. Around the necrotic focus and the arteriole, and closely resembling the ballooned cells of the central zone, are concentric aggregates of swollen cells.

This figure is believed therefore to show central fibrinoid necrosis of a glomerular tuft, the cells of which have swollen in the way characteristic of D.C.A. overdosage. The illustration also serves to demonstrate the focal nature of the vascular damage. It should be compared with figures 81 and 82 which show fibrinoid necrosis of afferent arterioles in the kidney from a rat with malignant renal hypertension. Picro-Mallory. x 500.
Figure 22.

Renal lesions due to D.C.A.

In this figure more extensive fibrinoid necrosis is seen involving an arteriole. An intense surrounding cellular reaction has occurred. From a study of this and the preceding 3 illustrations the difficulty of distinguishing vascular from purely glomerular damage will be appreciated. Part of a normal glomerulus is shown on the right and indicates the size of the central lesions. Nearby tubules show only slight dilatation.

Picro-Mallory. x 400.
Renal lesions due to D.C.A.

The present illustration shows a focus of fibrinoid around which is a concentric aggregation of swollen cells. This process closely resembles the disintegration of a glomerulus.

Figure 23.

Micro-Mallory. × 400.
Renal lesions due to D.C.A.

The definition of the glomerular tuft shown in the present figure is less clear than in those shown previously. It resembles more nearly those seen in earlier illustrations where protein-containing fluid has escaped into the subcapsular space and between the cells of the glomerular tuft. Nearby tubules are dilated and contain proteinaceous material. Proliferating tubular epithelial cells are seen lying in polypoidal fashion within the lumina of the tubules at the lower right margin.

Picro-Mallory. x 480.
Figure 25:

Renal lesions due to D.C.A.

In the present illustration the remains of a glomerular tuft are shown. There is a dense central focus of fibrinoid material. The surrounding concentrically arranged distended cells merge imperceptibly into the nearby renal tissue.

Picro-Mallory. x 500.
Figure 26.

Renal lesions due to D.G.A.

Similar glomerulus stained by the periodic acid-Schiff method to show the Schiff-positive central focus of fibrinoid and the surrounding cellular reaction. Near the lower part of the necrotic area an apparently intact arteriole is seen. The cellular reaction surrounding the glomerulus extends to involve the nearby tubules, some of which are slightly dilated.

P.A.S. x 430.
Renal lesions due to D.C.A.

Low power view to show the relationship between vascular fibrinoid necrosis, glomerular disintegration, and the related cellular reaction. This appearance is typical of the advanced reaction to large amounts of D.C.A. On the left a glomerular tuft is enlarged and its cells ballooned. At the upper right margin an artery may be followed to the point at which it suddenly undergoes fibrinoid necrosis. Between this point and the enlarged glomerulus is a further focus thought to represent the disintegration of a glomerular tuft.

Picro-Mallory. x 220.
Figure 23.

Renal lesions due to D.C.A.

Glomerulus from a kidney of a rat given excess D.C.A. showing fibrinoid change in the tissue around the afferent arteriole. The tuft itself, however, is almost intact, but the epithelial cells of the related tubule contain numerous hyaline droplets. At the left upper margin dilatation of a collecting tubule is seen with intratubular bulging of its cells. There is only slight dilatation of the proximal convoluted tubules.

Micro-Mallory. x 500.
Figure 29.

Renal lesions due to D.G.A.

Fibrinoid within the wall of a renal afferent arteriole, the media of which is thickened. Around the vessel there is a scanty cellular reaction. The nearby tubules are dilated.

Picro-Mallory. x 1000.
Figure 30.

**Renal effects of B.C.A.**

Low power view to show a dividing artery and its branches in the kidney of an animal given excess rapidly absorbed B.C.A. One of these vessels leads directly to a focus of fibrinoid necrosis surrounded by proliferating endothelial type cells. To the left of the figure a larger focus of fibrinoid probably represents disintegration of a small blood vessel. The cellular reaction surrounding these vessels closely resembles that seen about the glomeruli.

Picro-Mallory. x 130.
Figure 31.

Renal effects of excess A.C.A.

One of the arteries from the kidney shown in the previous illustration. A section has been stained to show the elastic fibres of the wall. Those on the lower right are intact; explosive disintegration of the vessel is seen and the elastic fibres disappear towards the left, where they are lost in a focal reaction of the type shown in the previous figure.

Gomori’s Aldehyde-Fuchsin. x 600.
Figure 32.

**Renal influence of D.C.A.**

Fibrinoid necrosis of the afferent arteriole of a glomerulus showing slight D.C.A. changes. The tuft is a little enlarged, but the response as a whole is similar to that of malignant hypertension produced by a variety of means. Compare Figures 31 and 32.

*Micro-Mallory.* x 1000.
In the present illustration the glomerular tuft shows slight changes only. The related arteriole however has undergone almost complete fibrinoid necrosis, which appears to stop short at the base of the glomerulus.

This appearance is less common than those shown in Figures 5 et seq., the majority of glomeruli of the kidneys of animals treated with excess D.C.A. show generalised cellular dilatation.

Micro-Mallory. x 480.
Figure 34.

Renal lesions of D.C.A.

Lower power view to show again the relationship between the apparently normal artery just beyond its point of bifurcation and a focus of fibrinoid, probably a disintegrating arteriole. A single relatively intact glomerulus is present and shows moderate enlargement and cellular dilatation. Throughout the field there is widespread proliferation of dilated endothelial type cells.

Micro-Mallory. x 340.
Figure 35.

**Glomerular changes caused by D.C.A.**

This figure illustrates the disintegration of an arteriole at its point of entry into a disrupted glomerulus. The artery is shown in the lower left hand corner with almost entirely intact elastic laminae. From its upper margin a vessel takes origin, and leads to a necrotic mass of fibrinoid lying among a widespread cellular reaction similar to those shown in the previous illustration.

*Gomori's Aldehyde-Fuchsin. x 350.*
Tubular changes caused by D.C.A.

This figure and those on succeeding pages illustrate the tubular reactions found in the kidneys of animals subjected to prolonged excess D.C.A.

Tubular dilatation is extreme. It affects principally the collecting tubules of the cortex. The convoluted tubules are involved to a lesser degree but some contain proteinaceous debris.

Picro-Mallory. x 220.
The present illustration shows the extensive and widespread proteinuria which is characteristic of the late stages of prolonged D.C.A. overdosage. The staining reactions of the protein-containing casts are variegated but the majority are hyaline in nature. Many of the collecting tubules shown in the present illustration are lined by swollen vacuolated cells. The limbs of Henle are affected only slightly.

Micro-Mallory. x 260.
Figure 36.

Tubular lesions caused by D.C.A.

The present illustration shows the degree of tubular dilatation which is common in animals treated with slowly absorbed D.C.A. for a prolonged period. In the lower part of the figure two collecting tubules are severely dilated while the proximal convoluted tubules (left upper margin) and the distal convoluted tubules (upper centre) are less severely involved. Cytological changes in these tubules are relatively slight.

Hasson. x 500.
Tubular changes caused by D.C.A.

Higher power view to show the cellular changes which occur in the earlier stages of D.C.A. overdosage. There is slight dilatation of these proximal convoluted tubules and occasional protrusion of nuclei or cytoplasm within the lumen of the respective tubules.

Masson. x 1000.
Figure 40.

Tubular changes caused by D.C.A.

Lower power view of similar field to show the general state of the tubules in the early stages of excess absorption of slowly acting D.C.A. A glomerulus shown in the lower part of the figure is almost intact, although slightly enlarged. Both convoluted and collecting tubules are slightly dilated and in some there is cytoplasmic and nuclear intratubular protrusion.

Masson. x 500.
Figure 41.

Tubular changes caused by D.C.A.

Low power view of severely involved glomerulus
(left centre), with ballooning of the cells, to show transudation
of protein into the glomerular subcapsular space and thence
into the corresponding tubules, many of which are dilated.

Picro-Mallory. x 220.
Figure 42.

Tubular changes in kidney from animal given hydralazine, for comparison with those of severe D.C.A. overdose.

In this illustration the greater part of the glomerular tuft on the right has undergone fibrinoid necrosis. The corresponding tubule contains proteinaceous fluid - its cells are dilated and granular and hyaline droplet change is recognizable. The appearances should be contrasted with those in the previous illustration.

Picric-Mallory. x 330.
Figure 42.

Tubular changes caused by D.C.A.

High power view of glomerulus to show transudation of protein among the glomerular cells and within the subcapsular space. The related tubule (upper right corner) contains protein of the same nature. Its cells are dilated, vacuolated and show conspicuous hyaline droplet change.

Picro–Mallory. x 500.
**Figure 4A.**

**Tubular changes caused by D.C.A.**

Those parts of the glomerular tufts shown in the upper and lower parts of the figure appear normal, but the convoluted tubules are dilated and contain proteinaceous fluid, the margins of which show retraction due to fixation. In the lower left part of the picture a dilated collecting tubule lies next to a group of convoluted tubules, the cells of which show prominent intratubular protrusion of cytoplasm and nuclei.

*Micro-Mallory. x 270.*
Figure 45.

The effects of rapidly-absorbed, excess P.G.A.

Further field to show involvement of a glomerulus, and the escape of protein-containing fluid into the subcapsular space and thus into the corresponding tubule. The cells of the glomerulus at the upper left corner are dilated; the collecting tubules at both margins are dilated and their cells occasionally protrude into the tubular lumen.

*Micro-Mallory.* x 240.
The cytological changes due to slowly-absorbed D.G.A.

High power view to show detailed cellular changes characteristic of the electrolyte disturbances occurring with D.G.A. There is slight dilatation of these proximal convoluted tubules; the cytoplasm of the epithelial cells in many places protrudes into the tubular lumen; many of the nuclei lie at the internal margins of the cells - they are thus cut across in section and are seen (particularly in the upper tubule shown in the illustration) lying apparently free within the lumen.

Figure 16. Micro-Gallory. x 1000.
Figure 47.
The cytological changes due to slowly-absorbed D.C.A.

In this illustration the tubular changes resulting from the electrolyte disturbances of excess D.C.A. are clearly shown. There is dilatation of collecting tubules (for example near the upper left corner of the figure), dilatation of the proximal convoluted tubules (in the lower part of the figure) and slightly of the distal convoluted tubule (lower right corner). In the proximal convolutions epithelial cell nuclei are seen protruding within the tubular lumina and the cytoplasm of many of these cells is separated and prolonged.

Micro-Mallory. x 600.
Figure 13.

Tubular effects of excess slowly-absorbed D.C.A.

In the large cluster of proximal convoluted tubules shown in the centre and lower part of the figure there is slight tubular dilatation, separation, particularly of the internal margins of the cells, and protrusion of the cellular nuclei within the lumen of the tubules. In the upper left part of the figure a distal convoluted tubule is seen running towards the upper margin - its cells show similar but less severe changes.

Picro-Mallory. x 500.
In this section, the cellular changes seen in the previous two illustrations are again illustrated. Both proximal and distal convoluted tubules can be distinguished, the cells of the former showing more severe disorganisation than those of the latter. Both are dilated.
Figure 50.

Tubular effects of excess D.G.A.

Slightly higher power view to show more severe dilatation of tubules — the presence of recognisable intercellular boundaries indicates that these are in fact distorted collecting tubules, although their cytoplasm stains rather more darkly than usual. In the most central tubule, in its uppermost part, a single interstitial collecting tubule cell can be seen projecting into the tubular lumen in the classical dumb-bell-like fashion described by Oliver et al (1957). This is one of the changes described by Oliver as characteristic of potassium depletion. The vacuolation of collecting tubule cells which he describes is not evident in this illustration.

Micro-Mallory. x 550.
Figure 51.

Tubular effects of excess D.C.A.

A similar magnification to show the appearances seen in many of the distal convoluted tubules in D.C.A. overdosage. Generally the distortion of the distal convoluted tubules is less severe than that of either the proximal convolutions or of the collecting tubules, a finding which does not concur with the suggestion of Selye that the tubular changes in this condition result from obstruction of the collecting tubules by hyaline casts.

Micro-Mallory. x 550.
Figure 52.

Tubular effects of excess D.C.A.

Low power view to show characteristic appearances of the collecting tubules of many renal areas in prolonged D.C.A. overdosage. There is dilatation and widespread tubular vacuolation. The appearance of these tubules is strongly reminiscent of those seen concurrently in many glomerular cells. Both changes are believed to be the result of osmotic disturbances.

Micro-Mallory. x 260.
Figure 52.

Tubular effects of excess D.S.A.

Higher power view of same field to show in more detail the dilatation and vacuolation of the collecting tubule cells.

Ficro-Mallory. x 600.
Figure 54.

Tubular effects of excess D.C.A.

Further high power view of collecting tubule which runs diagonally across the illustration. Vacuolation of the tubular cells can be distinguished, the lumen is dilated and into it protrude cells which begin to show polypoidal-like proliferation similar to that described in potassium depletion.

Micro-Mallory. x 550.
Tubular effects of D.C.A. excess.

Higher power view of collecting tubule to show in detail the hyaline changes frequently seen as a result of the osmotic disturbances occurring in prolonged D.C.A. overdosage. The tubule is dilated and within the lumen droplets of protein-containing material lie apparently free. The normally smooth inner border of the tubule is replaced by a serpiginous outline, the result of intratubular cellular cytoplasmic protrusion.

The overall result of these changes is a great increase in the internal tubular surface area.

Picro-Mallory. x 900.
Figure 56.  

Experimental Series II.

Glomerular influence of hydrallazine

In this and the subsequent illustrations the evolution of the glomerular lesions brought about by hydrallazine is demonstrated.

This figure shows a characteristic hemiglomerular segmental necrosis. It is accompanied by disintegration of one half of the tuft. The other half is preserved intact. Protein-containing fluid has escaped into the subcapsular space.

These lesions are focal in distribution and are not accompanied by vascular changes.

Micro-Mallory. x 600.
Figure 57.

**Glomerular influence of hydrallazine**

A similar glomerular lesion in which aneurysmal dilatation of the damaged glomerular loops is conspicuous. Fibrinous material has escaped between the capillary loops and permeability of the vessels has led to the presence of protein-containing fluid in the subcapsular space.

That part of the tuft seen on the left is largely intact.

*Masson. x 600.*
Figure 58.

**Glomerular influence of hyalalgine**

In this figure a further acute hemiglomerular necrosis is seen. The lesion is composed largely of fibrinous material, but at the upper margin a dilated capillary loop is seen. The remainder of the tuft is intact. The blood vessels are normal, but part of a convoluted tubule seen at the right margin of the illustration shows hyaline droplet change.

*Picro-Mallory* x 600.
A further acute segmental glomerular necrotic lesion is shown in this illustration. Rather more than half of the tuft is intact; the remainder is occupied partly by damaged capillary and epithelial cells and partly by an accumulation of fibrin and red blood cells. It is notable in this as in many other examples of this lesion that the occurrence of the necrosis has not led to complete disintegration of the basement membrane of the tuft. The integrity of this basement membrane implies in most instances that protein-containing fluid and blood does not escape into the subcapsular space.

Figure 59.

**Glomerular influence of hydralazine.**
Figure 60.

**Glomerular influence of hydralazine**

A focal necrotic glomerular lesion of similar type to that shown in the previous illustration. Rather more than half the tuft is apparently involved, but the remainder is intact.

*Picro-Mallory. x 600.*
Figure 61.

Glomerular lesions precipitated by hydralazine.

In this illustration the focal distribution of the necrotic glomerular lesions caused by hydralazine is clearly shown. On the left an enlarged glomerulus is seen, half of which has undergone necrosis, now being occupied by fibrinous material and by cellular debris. On the right an enlarged glomerulus of largely normal structure is shown.

It is important to observe that the structure of the enlarged glomerulus shows little evidence of the changes found when excess D.C.A. is given in rapidly absorbed form. Glomeruli of this type accompany the moderately severe tubular changes found in the kidneys of animals given slowly absorbed D.C.A. for long periods.

Micro-Mallory. x 400.
The focal glomerular lesions caused by hydralazine

The random distribution of the hydralazine-induced focal glomerular necroses is clearly shown in this figure. Two adjacent tufts are seen, both apparently completely destroyed. The completeness of destruction may in part be due to tangential sectioning of the tufts.

The glomerulus on the left shows aneurysmal capillary dilatation and fibrinoid necrosis, while that on the right is occupied by granular fibrinous material and by cellular and nuclear debris.

Ficro-Mallory. x 500.
Focal distribution of lesions caused by hydralazine

Low power view which again serves to emphasise the focal distribution of hydralazine glomerular necroses. Two almost normal and one partly necrotic glomeruli are shown.

Picro-Mallory. x 240.
Figure 64.

Glomerular necrosis caused by hydralazine

This illustration shows a characteristic hemiglomerular necrosis. Notice that the convoluted tubules seen at the right lower margin show hyaline droplet change, a finding frequently seen in the tubules related to a partly necrotic glomerulus. Observe also that the uninvolved part of the glomerular tuft does not show the lesions of D.C.A. overdosage.

Picro-Mallory. x 600.
Figure 65.

Glomerular changes caused by hydralazine

High power view to show early organisation of a hemiglomerular necrosis. The lower segment of the glomerulus contains hyaline droplets and distorted epithelial and endothelial cells which form a crescent-like structure adherent to the capsular epithelium.

Such an appearance is exceptional in the evolution of the hydralazine lesion.

Micro-Mallory. x 500.
Figure 66.

**Hemiglomerular necrosis due to hyaluronic**

The fibrinous material in this hemiglomerular necrosis shows early signs of replacement fibrosis. Polymorphonuclear leukocytes and red blood cells are fewer in number than in the earlier illustrations, there is less fibrinoid material and fibroblasts are beginning to appear.

*Masson.* x 600.
Figure 67.

Renal lesions caused by hyaluragine

The glomerulus shown in this illustration is unusual in that two segments appear to be involved. That in the upper part of the figure shows fibrinous material, disorganisation, and hyaline droplet change. That in the lower part forms an early epithelial crescent, binding the tuft to the capsule.

Micro-Mallory. x 500.
Figure 66.

Renal lesions caused by hydrallazine

The glomerular tuft shown in this figure is widely disorganised. Only at the lower margin do normal capillaries remain. The severe hyaline droplet change often seen in this stage of the lesion is shown in the convoluted tubular cells on the left.

Masson. x 600.
Figure 62.

Renal lesions caused by hydralazine

Organisation and replacement fibrosis of a hemiglomerular necrosis is shown in this illustration. The right half of the tuft is intact. The left half is occupied by proliferating fibroblasts, and adheres to the capsular epithelium over an area which includes eosinophilic proteinaceous fluid.

The nearby convoluted tubules show moderately severe osmotic changes.

Miro-Mallory. x 600.
Figure 76.

Renal lesions caused by hydralazine

Organisation of a hemiglomerular necrosis has occurred in the tuft shown in this figure - the glomerular scar occupies much of the upper part of the tuft. As usual, the tuft does not adhere to the capsular epithelium and there is no crescent formation.

Note the dilated collecting tubule (right mid-zone of figure) and the severe cellular changes shown principally in the proximal convoluted tubules.

Masson. x 500.
Figure 71.

Renal lesions due to hydralazine

A further segmental glomerular scar is shown in this illustration - like many seen in these animals it adheres to the capsular epithelium.

Tubular changes closely resemble those seen in the previous illustration.

Masson, x 500.
Figure 72.

Renal lesions caused by hydralazine

This figure shows a further central segmental glomerular scar. The remainder of the tuft appears intact. The tuft adheres to the capsular epithelium over the surface of the scar tissue and in this region protein-containing fluid is still present in excess.

Masson. x 600.
**Figure 73.**

**Effects of hydralazine on the kidney**

High power view of glomerulus showing a lesion of a typical type. The crescent-like formation in the upper part of the illustration is accompanied by hyaline droplet change and by proliferation of the capsular epithelial cells at the lower left margin.

This lesion is regarded as a variant of those seen commonly following the prolonged administration of hydralazine.

*Picro-Mallory. x 500.*
Figure 7A.

**Experimental Series IV.**

**Renal ischaemia and malignant hypertension**

In this figure and in those which follow it the effects of ischaemia and of malignant hypertension are shown. The changes in these kidneys have been induced by the unilateral application of renal arterial clips.

This figure shows glomerular crowding (the result of atrophy of tubules).

The appearances are those of partial infarction and often result from incomplete constriction of a renal artery.

*Picro-Mallory* x 240.
Figures 75.

Renal ischaemia; malignant hypertension.

Similar field from a section of the same kidney stained to show the elastic walls of the arteries. The inter-relationship of these arteries, and of the numerous glomeruli serves to indicate the degree of tubular and interstitial tissue atrophy which results from partial infarction.

Gomori's Aldehyde-Fuchsin. x 240.
Figure 76.

Renal changes in malignant hypertension

Crescent formation in this glomerulus is recent, and the result of the escape of protein-containing fluid into the subcapsular space. This is an appearance seen frequently in the glomeruli of kidneys in malignant hypertension.

Fioro-Mallory. x 550.
Figure 77.

Renal changes in malignant hypertension due to renal ischaemia

Ischaemia has caused capsular epithelial proliferation in this glomerulus from an animal with malignant hypertension. There is fibrinoid necrosis of part of the afferent glomerular arteriole and several of the glomerular capillaries contain hyaline thrombi.

Micro-Mallory. x 500.
Renal changes in malignant hypertension due to renal ischaemia

Part of a section of a kidney from an animal with malignant hypertension. The glomerulus on the left shows widespread hyaline capillary thrombi and fibrinoid change. It is much enlarged and adheres to the capsular epithelium.

The glomerulus on the right has undergone ischaemic fibrosis and appears to be functionless.

Micro-Mallory. x 550.
Figure 79.

Renal changes in malignant hypertension due to renal ischaemia

The present illustration shows the nature of tubular and glomerular changes frequently seen in malignant hypertension accompanying renal ischaemia. There is atrophy and disintegration of tubular epithelium, and crowding of glomeruli, many of which show either severe ischaemic fibrosis or the manifest effects of malignant hypertension; these include fibrinoid vascular necrosis and the presence of hyaline thrombi within the capillaries.

Micro-Mallory. x 260.
Figure 80.

Renal changes in malignant hypertension due to renal ischaemia

The glomerular tuft shown in the present illustration has undergone segmental necrosis. This is a change seen occasionally in malignant hypertension in which, unlike hydralazine overdosage, it is invariably accompanied by fibrinoid arteriolar necrosis.

The lesion shown here is the only hemiglomerular necrosis found in the present experimental series. It is indistinguishable from those of hydralazine overdosage apart from the associated vascular changes.

Micro-Mallory. x 600.
Fibrinoid necrosis of the afferent glomerular arteriole is seen in this illustration. This is one classical effect of experimental malignant hypertension. The glomerular response clearly bears no morphological relationship to that seen as a result of the administration of hydralazine, but similar changes accompany severe B.C.A. overdosage. From the latter it is distinguished by the absence of the characteristic cellular ballooning and from the former by the involvement of the whole glomerulus and by the presence of arteriolar damage.
This figure shows a further lesion of the same character. There is glomerular ischaemia and afferent arteriolar fibrinoid necrosis. The appearances are characteristic of malignant experimental hypertension due to renal ischaemia.

Figure 82.

Renal changes in malignant hypertension due to renal ischaemia

Micro-Mallory. x 500.
The influence of D.C.A. and unilateral nephrectomy on renal size

The three kidneys seen in this illustration are from animals of group 24, experiment II(a). Each animal was treated with daily injections of D.C.A. and by the administration of 1% sodium chloride following unilateral nephrectomy.

The blatant effects of the hypertension following excess D.C.A. were prevented by the daily injection of hydrallazine. It is clear, however, that this has not influenced the great increase in size of the kidneys which invariably follows D.C.A. overdosage and which is due principally to tubular dilatation.

The kidney shown on the left is from an animal dying within a few days of starting treatment, that in the centre from an animal surviving two months, and that on the right from an animal surviving three months. The latter kidney is rather more than twice the size of a normal control of similar age.

Micro-Mallory. x 5.