other the cause was not discovered. Both showed a slight temporary increase in blood pressure and improvement following the administration of 800 c.c. of the 4% solution. Both subsequently died.

Brief summaries of two representative cases follow:

CASE 1

Female, aged 44 (C.G. No. B38234). This patient accidentally plunged her forearm through a window pane and suffered a severe laceration and severance of the radial artery. She was admitted to hospital about two hours after the accident in a state of severe collapse as a result of profuse hæmorrhage; she was semiconscious, very pale; the skin was cold and moist; the pulse rate was barely perceptible, 50 per minute and the systolic blood pressure 45 mm. of mercury.

The rapid intravenous administration of 500 c.c. of 5% glucose in physiological saline, resulted in slight improvement. This was immediately followed by the infusion of 800 c.c. of 6% isinglass over a period of twenty minutes, following which she was markedly improved; she was alert, the pulse rate was 60 per minute and the blood pressure 120/72; the hæmoglobin was 38%. An anæsthetic was given, the radial artery ligated and the wound sutured.

Although the patient's condition was satisfactory and the blood pressure was well maintained, a transfusion of 500 c.c. of blood was given five hours after the administration of isinglass because of the anæmia.

Subsequently the patient progressed well. Her temperature never rose above 100° F. Four days after the accident the hæmoglobin was 48% and the red blood count 2.8.

CASE 2

Female, aged 49 (L.S., No. B20689). Diagnosis: (1) thermal burn (40% of body surface); (2) manic depressive psychosis.

This patient was admitted to hospital in a state of moderately severe shock about four hours after the infliction of the burn; pulse rate 144, blood pressure 95/80, hæmoglobin 108% and hæmatocrit 47%. During the next hour she was given 250 c.c. of human plasma. At the end of that time her blood pressure was 85/70 and hæmoglobin 117%. No more plasma was given.

Administration of a 4% solution of isinglass was commenced two hours after admission and a total of 3,800 c.c. were infused during the next twenty-four hours. Her hæmoglobin fell to 80% and the blood pressure rose to 200/110. She then vomited about one pint of dark brown fluid and the blood pressure fell toward normal and subsequently was never found at a level higher than 165/90. No further infusions of isinglass were required as the hæmoglobin remained at levels below 80%.

The serum proteins, which were 7.8% on admission, fell to 4.8% (albumin 2.8%, globulin 2.0%) two days after admission. Subsequently the level slowly recovered and the total proteins were 7.3% twenty-two days after admission.

During the first few days the urine volume was low, its specific gravity varied up to 1.041, albumin, sugar and a trace of urobilin were found and occasional granular casts were seen. The blood non-protein nitrogen rose to 53 on the second day. Subsequently the blood non-protein nitrogen and urinalysis were normal except that a trace of albumin continued to be found in the urine for a time. On the second day the blood hæmoglobin was 84%; red cell count 4.3 million, white blood count 21,000, blood smear showed no significant change except for an increase of polymorphonuclear cells. Blood chlorides, CO_2 combining power and Van den Bergh were normal.

The burns on the torso were treated by 10% tannic acid spray and those on the extremities by application of 5% sulfathiazole emulsion. Although the patient survived the period of burn shock and toxæmia, she died six weeks later as a result of wound sepsis.

SUMMARY AND CONCLUSIONS

Purified, powdered isinglass, dissolved in physiological saline solution, in concentration of 4 to 7%, was administered intravenously to a total of 61 patients. It was given to 51 patients to detect the occurrence of pyrogenic or other toxic effects and to ten patients in the treatment of shock and acute hæmorrhage.

When properly prepared, isinglass solution appears to be a safe blood substitute. In a small proportion of cases a slight or moderately severe febrile reaction occurred. In none of the patients to whom it was administered for the treatment of shock did any type of unfavourable reaction, febrile or otherwise, occur.

In a small series of cases of shock, the intravenous administration of solutions of isinglass appeared to be of value.

PATHOGENETICAL CORRELATIONS BETWEEN PERIARTERITIS NODOSA, RENAL HYPERTENSION AND RHEUMATIC LESIONS*

By Hans Selye, M.D., Ph.D., D.Sc., F.R.S.C. and E. Irene Pentz, M.Sc.

Montreal

THE purpose of this communication is to report upon experiments which revealed close pathogenetical relationships between periarteritis nodosa, nephrosclerosis, arterial hypertension and the rheumatic lesions.

In 1866 Kussmaul and Maier[1] discovered a disease which they described under the title "Concerning a Curious Hitherto Not Described Disease of the Arteries (Periarteritis Nodosa) Which is Accompanied by Bright's Disease and Rapidly Progressing Muscular Paralysis". We recently found that under certain experimental conditions a hormone of the adrenal cortex can elicit arteritis nodosa in animals and that the outstanding accompaniments of this artificially induced disease are the same as those to which, 77 years ago, Kussmaul and Maier gave prominence by special mention in the title of their

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article on the spontaneously recurring malady of man.

Concerning the literature on arteritis nodosa, the reader is referred to the excellent summary of Motley,[2] in which 215 cases have been reviewed. Here we only wish to discuss those communications which throw some light upon the pathogenesis of the disease and its relationship to nephrosclerosis, hypertension, and certain rheumatic manifestations.

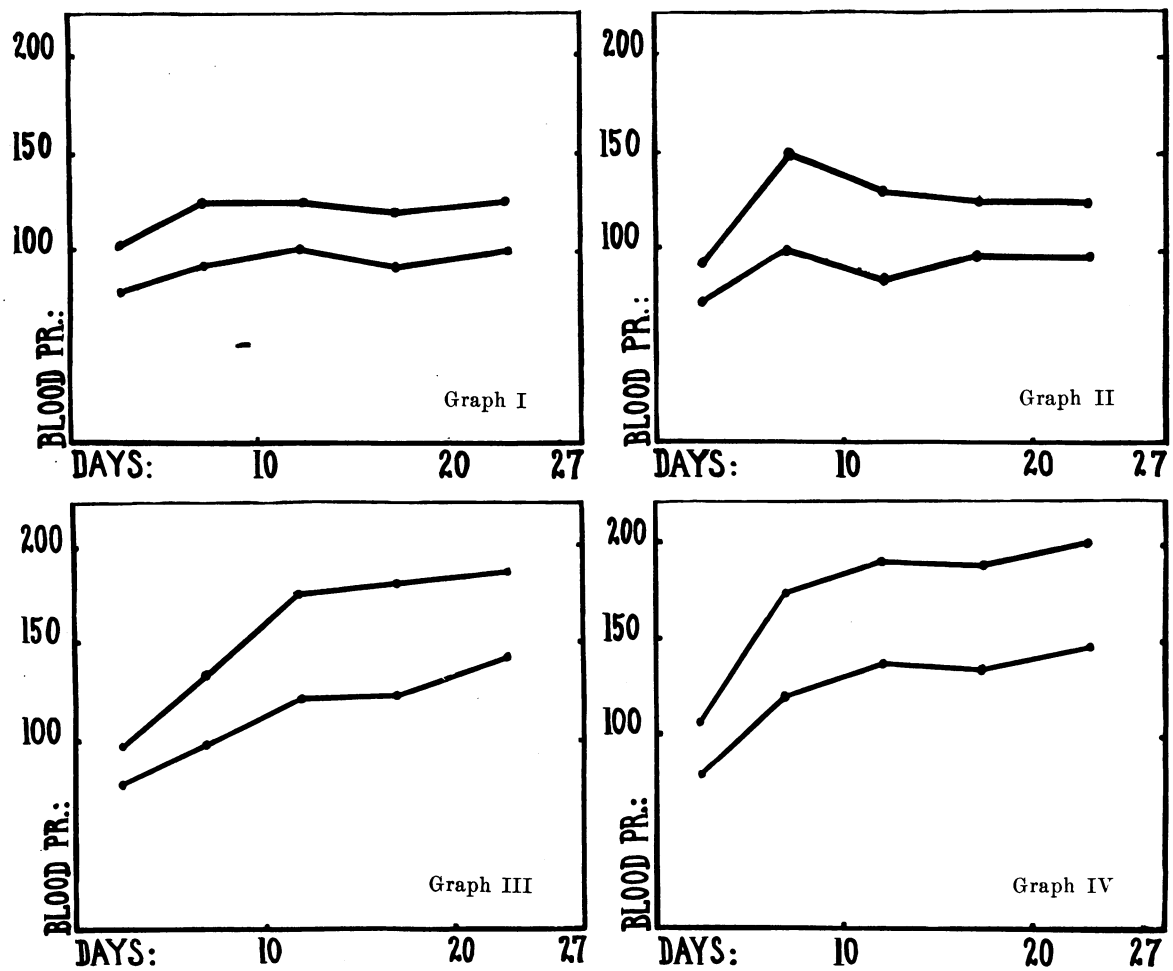
PATHOGENESIS

The fact that periarteritis nodosa is very frequently accompanied by obvious signs of nephrosclerosis and hypertension, is evident, even from the most cursory study of the published cases.[3, 4, 5] It has also been emphasized that, conversely, the arterial lesions in the kidneys of patients suffering from malignant hypertension are histologically similar to arteritis nodosa. Haining and Kimball[6] pointed out in their review on periarteritis nodosa that "when the kidney is chiefly involved, the course is indistinguishable from essential hypertension with nephrosclerosis". They also emphasized, in agreement with many other workers, that the mesenteric arteries are most commonly affected.

The relationship with rheumatic fever is less clear. The histological appearance of the arteritic nodules is somewhat reminiscent of rheumatic foci, and the fact that both these lesions are often found along the course of blood vessels in the heart and in the subcutaneous tissue may be interpreted as tentative evidence of such a relationship. The comparatively frequent association of rheumatic fever with manifestation of periarteritis nodosa is much more striking. Klinge[7] stated that ". . . there also is a 'rheumatism' of the arteries and veins which in its final stage gives the impression of arteritis nodosa. . . ." Friedberg and Gross[8] reported four cases of periarteritis nodosa associated with rheumatic fever and rheumatic heart disease; the latter being confirmed by the presence of Aschoff bodies in the myocardium. They collected many similar additional cases from the literature. More recently, Spiegel[9] described fifteen cases of periarteritis nodosa with autopsy reports. Four of these had had manifest rheumatic fever.

Experimental work also suggests that intimate relationships exist between periarteritis nodosa, renal hypertension and rheumatic-allergic manifestations. Klinge[10] succeeded in producing a condition similar to rheumatic arthritis by repeated injections of horse serum in the rabbit. He emphasized that there was an accompanying arterial lesion which "resembled most closely that seen in the arteritis nodosa of man and animals". v. Haun[11] transmitted the disease from a proved case to guinea pigs by blood transfusion; hence, he believed the condition to be infectious. Harris[12] injected a mush of arteritis nodule tissue into rabbits, and these subsequently also developed the disease. Since passage through a Berkefeld N filter did not inactivate tissue extracts, he concluded that the condition is infectious and is caused by a virus. As no controls were done with mush of normal tissues, the significance of this experiment is rather doubtful, since several other investigators produced either typical periarteritis nodosa or malignant nephrosclerosis by treatment with various proteins. Thus Metz[13] elicited periarteritis nodosa by streptococcus injections, but found that following sensitization, cattle serum produces the same effect. He also emphasized that some of his animals which received serum treatment exhibited histological changes of the rheumatic type and called attention to the frequent association of rheumatic and allergic conditions in man. By feeding a high protein diet to unilaterally nephrectomized rats, Blatherwick *et al.*[14] produced nephrosclerosis, with obliteration of the capsular space, dilation of the convoluted tubules and formation of hyaline casts. Similar changes have been elicited in the intact dog, cat, rabbit and guinea pig by repeated injections of horse serum or egg white.[15] More recently, Oberling[16] obtained comparable results by multiple intravenous serum injections in the rabbit and mouse. It is not within the scope of this communication to discuss the voluminous literature on the so-called "nephrotoxic" sera which are generally considered to be highly specific.[17]

Although, perhaps not quite relevant to our problem, we wish to point out, furthermore, that Meeker *et al.*[18] produced experimental atherosclerosis in rabbits by feeding high protein diets containing defatted casein. This diet was also active in aggravating the atheromatous lesions caused by cholesterol feeding. In conclusion, it may be mentioned that the self-observations of Bienstock,[19, 20] led him to conclude that human hypertension is also a form of "protein toxicosis".



Graphs I to IV.—Average blood pressure curves of the animals in the four groups of the experiment described in the text. The upper line represents the systolic and the lower the diastolic pressure.

LEGENDS FOR ILLUSTRATIONS

Fig. 1.—Macroscopic view of a normal intestinal loop (Group I). Note thin and regular mesenteric vessels.

Fig. 2.—Macroscopic view of an intestinal loop showing periarteritis nodosa (Group IV). Note numerous bead-like nodules along the mesenteric vessels.

Fig. 3.—Section through mesenteric insertion on intestinal wall (Group IV). Low magnification. Note thickening and infiltration of the transversely sectioned mesenteric artery.

Fig. 4. — Transverse section through mesenteric artery showing first stages of periarteritis nodosa (Group IV). Medium magnification. Note deposition of a thin layer of hyaline material underneath the somewhat irregular endothelial surface.

Fig. 5. — Transverse section through mesenteric artery showing a somewhat more advanced stage of periarteritis nodosa (Group IV). Note almost complete destruction of the endothelium with deposition of a fairly thick layer of hyalinized fibrin-like material on the vascular wall. The structure of the vessel is almost unrecognizable owing to heavy infiltration with leucocytes, many of which are eosinophilic. Some giant cells are also detectable. (Same magnification as Fig. 4).

Fig. 6. — Transverse section through mesenteric artery showing final stage of periarteritis nodosa (Group IV). Thick layer of hyalinized fibrin lines the lumen, the vessel walls underwent partial necrosis and, hence, appear somewhat homogeneous (same magnification as Fig. 4).

Fig. 7.—Arteritic nodule at the bifurcation of a mesenteric artery. Note thick layer of fibrin lining the vessel walls and a U-shaped thrombus which almost completely occludes the lumen (Group IV). The thrombus consists, mainly, of fibrin, platelets and leucocytes (same magnification as Fig. 4).

Fig. 8.—Degeneration of myocardial fibres with replacement by somewhat œdematous connective tissue (Group IV).

Fig. 9. — Typical Aschoff body in myocardium (Group IV).

Fig. 10.—Typical Aschoff body in subendocardial layer on a papillary muscle (Group IV). Note the characteristic eccentric location in the course of a blood vessel (in upper left corner of nodule). Centre of nodule consists of hyalinized material. Several Aschoff cells are detectable.

Fig. 11.—High magnification of a small Aschoff body in myocardium showing several slightly basophilic polymorphonuclear Aschoff cells with characteristic fringy cell borders (Group IV).

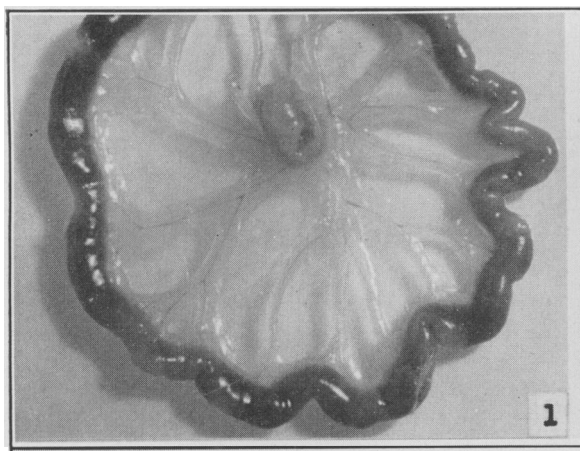
Fig. 12.—Pancreas with acute œdema of the stroma (Group IV).

Fig. 13.—Pancreas with marked hyalinization of the perivascular connective tissue (Group IV).

Fig. 14.—Control kidney (Group II). Note normal renal structure.

Fig. 15.—Nephrosclerotic kidney (Group IV) showing sclerosis of medium sized artery, greatly enlarged glomerulus with transudation of hyaline material into the capsular space and dilated convoluted tubules, many of which contain hyaline casts.

Fig. 16.—Subcapsular region of the kidney (Group IV) taken from the borderline of a sclerosed infarct area (right) and comparatively normal renal tissue (left).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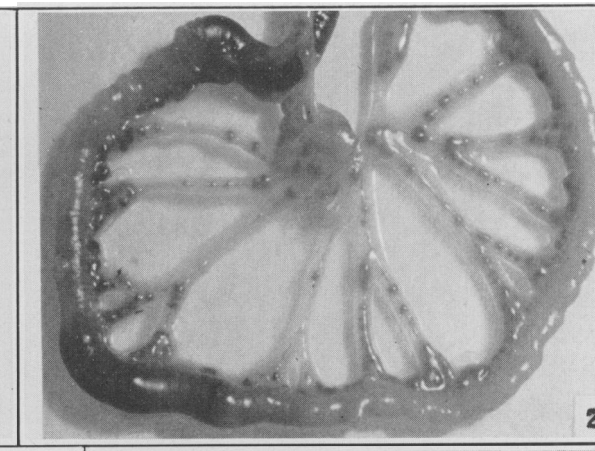
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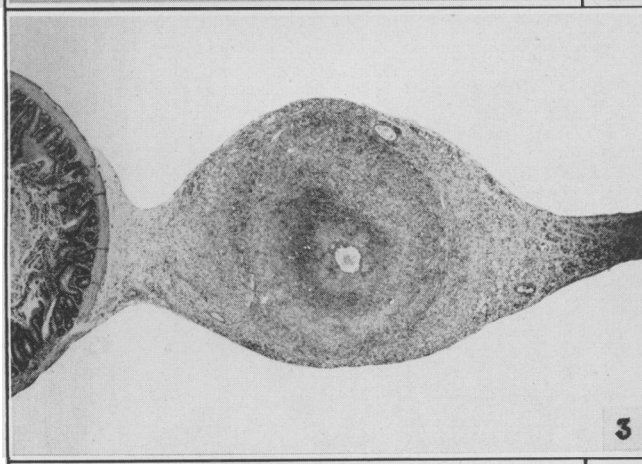
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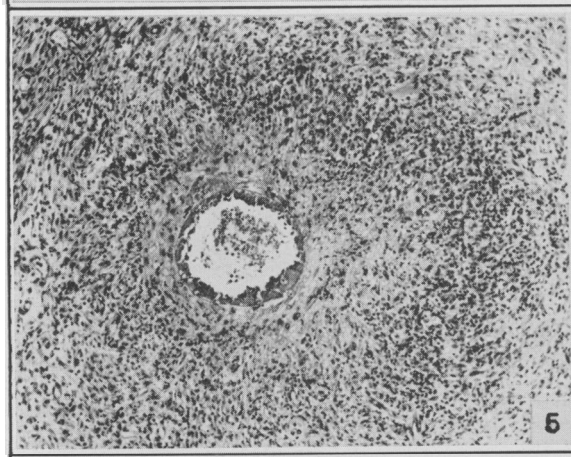
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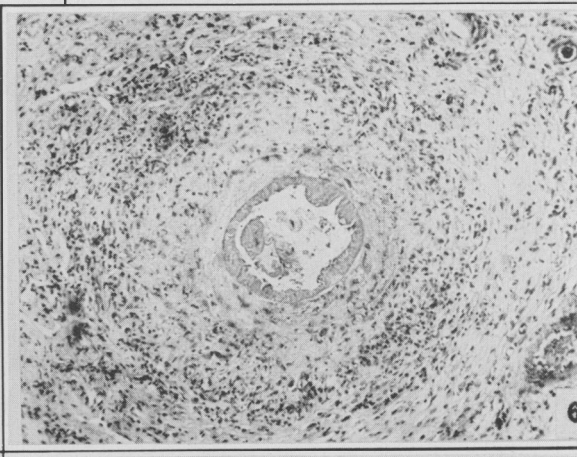
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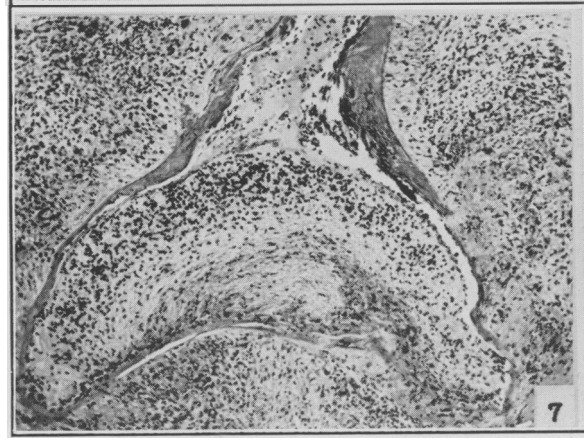
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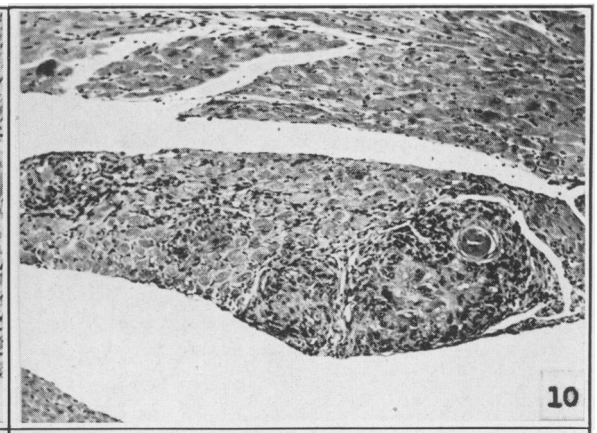
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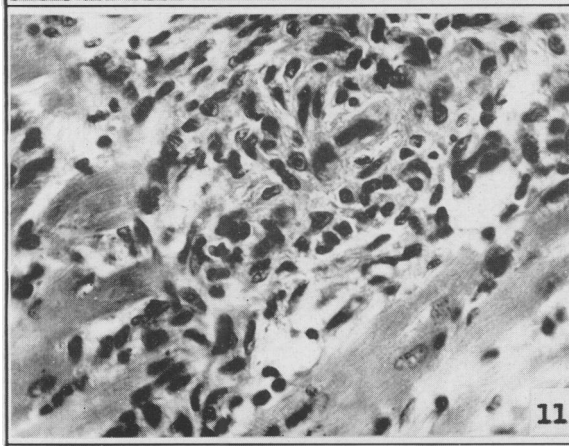
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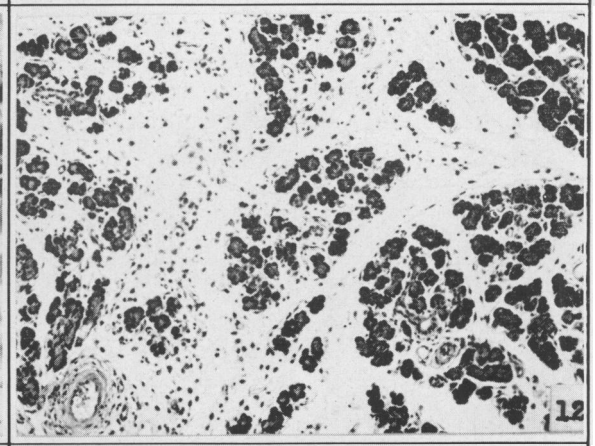
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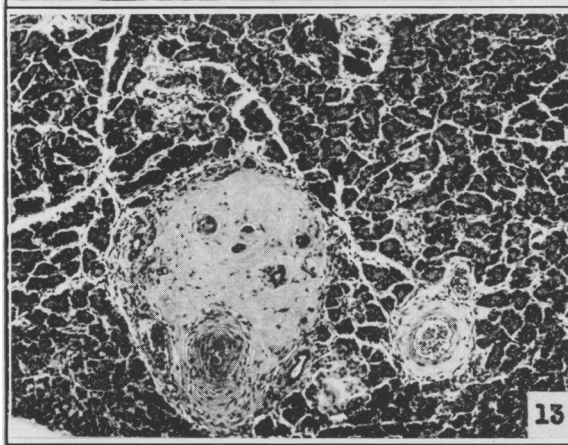
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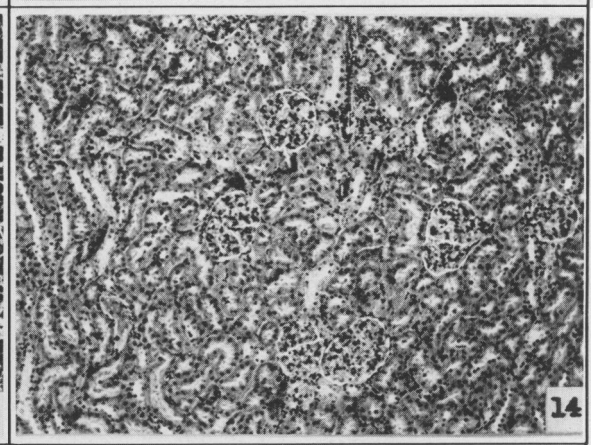
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Experiments performed in our laboratory during the last few years made it quite clear that certain steroid hormones exert a specific renotropic action[21, 22] and that depending upon the chemical structure of the steroids, they may produce tubular hypertrophy and hyperplasia with improvement in kidney function and no sign of hypertension (true renotropic action) or nephrosclerosis with hypertension (nephrosclerotic action).[23 to 26] The most active representatives of compounds exhibiting a true renotropic action are some of the androstane derivatives, while, among all steroids examined up to the present time, desoxycorticosterone acetate (D.C.A.) proved most potent in producing nephrosclerosis. Even extrarenal blood vessels are frequently damaged by D.C.A., and, among these, the medium-sized pancreatic arteries are especially severely affected.[27] Animals receiving large amounts of NaCl in their drinking water are markedly sensitized to these toxic actions of the corticoid hormone.[25, 26, 27] In animals with a highly developed central nervous system, such as the dog, and especially the monkey, acute administration of NaCl following chronic treatment with D.C.A. elicits certain motor disturbances characterized by tremor, choreiform twitches and convulsions, which are eventually followed by more or less widespread paralysis.[26]

Our present experiments show that the apparently so widely different manifestations of nephrosclerosis, hypertension, arteritis nodosa, the rheumatoid type of connective tissue nodule and certain choreiform nervous disturbances are actually closely related to each other, since they can be experimentally produced by a single agent, namely D.C.A.

EXPERIMENTAL

This experimental series was originally designed to increase the sensitivity of our present test method for nephrosclerotic activity. It was felt that ablation of one kidney might increase the D.C.A. sensitivity of the remaining renal tissue. The synergistic effect of NaCl and the greater sensitivity of females, in comparison with males, may now be regarded as definitely proved; hence, we felt that salt-treated partially nephrectomized female animals might be the ideal test object.

Four groups, each consisting of eight female albino rats, having an average weight of 98 grm. (range 80 to 133 grm.) were used. All four groups received a 1% NaCl solution instead of drinking water, and were fed "Purina Fox Chow" throughout the experiment. The rats of Group I were not otherwise treated and acted as controls. In Group II the left kidney was removed at the beginning of the experiment, but no other treatment was given. Group III was treated in the same way as Group I and Group IV as Group II, but in addition the animals of Groups III and IV were also given 3 mgm. of an aqueous crystal suspension of D.C.A. (concentration 30 mgm. per c.c.) subcutaneously twice daily. Three animals in Group III and two in Group IV died of pneumonia during the course of the experiment. The remainder was killed on the 27th day. The blood pressures of all animals were followed (using the technique of Friedman[30]) at approximately weekly intervals. The average values are summarized in Graphs I to IV. From these, it is evident that salt treatment in itself leaves both the systolic (upper line) and the diastolic (lower line) blood pressure essentially normal (Graph I). Unilateral nephrectomy causes a slight transitory rise which may be due to the compression ischæmia of the kidney which probably occurs during the first period of compensatory hypertrophy until the capsule stretches proportionally with the enlarged renal volume (Graph II). Combined treatment with NaCl and D.C.A. on the other hand, elicits a rise in both the systolic and the diastolic blood pressure. This rise continues throughout the experimental period and is accompanied by a gradual increase in the difference between the systolic and diastolic blood pressure, as shown by the progressive divergence of the two lines in Graphs III and IV. These changes are elicited by the hormone both in the intact (Graph III) and in the unilaterally nephrectomized (Graph IV) animals, but are more conspicuous in the latter.

MACROSCOPICAL FINDINGS

At autopsy, the most striking change was the presence of many reddish nodules along the mesenteric blood vessels. These were most numerous in the vascular territories of the small and upper large intestine, but were also detectable in the vessels of the rectum and stomach. Such nodules were present in all animals of Group IV, but only in one rat of Group III; hence, it appears that this action of D.C.A. is promoted by unilateral nephrectomy. In Groups I and II, the nodules were absent. From the

cases in which the lesions were comparatively slight, it was obvious that the blood vessel bifurcations are first affected. In more advanced cases, however, nodules were found at short intervals throughout the entire length of the vascular tree (Figs. 1 and 2).

The pancreas showed varying degrees of œdema in most D.C.A. treated animals, and this, again, was more pronounced in Group IV than in Group III.

Perusal of Table I indicates that the kidney was greatly enlarged in the D.C.A. treated groups. The weight of the remaining single

TABLE I.

ORGAN WEIGHT CHANGES FOLLOWING UNILATERAL NEPHRECTOMY AND D.C.A. TREATMENT

Groups	*Treatment*	*Kidney weight**	*Heart weight*	*Liver weight*
I	Control	1.36 grm. (1.20-1.48)	0.63 grm. (0.55-0.70)	7.52 grm. (6.04-8.30)
II	Unilaterally nephrectomized	0.96 grm. (0.80-1.28)	0.64 grm. (0.57-0.78)	6.18 grm. (4.31-7.72)
III	D.C.A.	2.13 grm. (2.09-2.19)	0.87 grm. (0.71-1.04)	7.91 grm. (6.36-8.77)
IV	D.C.A. Unilaterally nephrectomized	1.60 grm. (1.04-2.20)	0.94 grm. (0.77-1.15)	10.52 grm. (8.82-12.60)

*The figures listed in this column represent the combined weight of both kidneys in the case of intact animals (Groups I and III) and that of the one remaining kidney in the unilaterally nephrectomized rats (Groups II and IV).

kidney in unilaterally nephrectomized animals is, of course, above normal in any case, due to compensatory hypertrophy; however, this enlargement is especially marked following D.C.A. treatment, and the average weight of a single kidney in Group IV is greater than that of both kidneys in the control Group I. It is also noteworthy that in both D.C.A. treated groups, but especially in Group IV, the surface of the kidneys was very irregular and mottled. The larger spots were light, the smaller ones red, as in the "flea bitten" kidney of focal embolic glomerular nephritis. The heart was also enlarged in both D.C.A. treated groups and especially so in Group IV. The hearts of this group revealed small white spots reminiscent of minute anæmic infarcts.

The liver weight was not significantly increased in the D.C.A. treated intact animals of Group III, but was considerably above normal in Group IV. This hepatotropic action of the hormone will be considered in greater detail in a future publication. The bile duct of the rats in Group IV was somewhat thickened and dilated. At least in one case it contained concrements.

MICROSCOPICAL FINDINGS

Upon histological examination, the nodules seen along the course of the mesenteric vessels prove to be due to an enormous thickening of the vascular walls. The structural changes are strikingly similar to those seen in human cases of periarteritis nodosa. The earliest stages are characterized by the appearance of a thin layer of hyaline, eosinophilic material just underneath the endothelial lining, and during this stage the muscularis and adventitia are slightly thickened due to œdema and some connective tissue proliferation. During the subsequent development of the change, the subendothelial hyaline layer increases in height, and in many places, the endothelial lining is cast off. Almost the entire muscularis becomes necrotic or hyalinized and is heavily infiltrated by leucocytes, many of which are eosinophilic. Erythrocytes also appear in the connective tissue spaces of the muscularis and occasionally there are phagocytes containing a greenish-brown pigment, apparently derived from the hæmoglobin of decomposing red blood corpuscles. Large cells, often polynuclear — which bear a striking resemblance to the Aschoff cells of rheumatic nodules — are usually also quite prominent within this layer. Their cytoplasm is more tingible than that of the other mesenchymal elements and they have an indistinct fringy border. The adventitia shows similar, but less pronounced changes and usually remains œdematous even in the late stages. In the most advanced cases, the lumen of the blood vessel is completely, or almost completely, obliterated by the hyaline deposits on the vascular wall and by thrombi which consist mainly of fibrin and leucocytes. In these instances the changes resemble those characteristic of thrombangiitis obliterans. From this stage, the process may apparently proceed in one of two directions. In some cases the inflammatory lesions progress to heavy infiltration of the vessel walls with formation of pus and small abscess-like foci. In other cases the lesion heals by the formation of dense scar tissue with usually a rather hyaline matrix. Similar vascular lesions have also been observed with great frequency in the pancreas and the

kidney. The medium-sized muscular arteries are most severely affected, but especially in the mesentery, the kidney and pancreas the small arterioles and even the veins may reveal lesions of a similar type (Figs. 3 to 7).

The heart shows changes typical of rheumatic myocarditis and endocarditis. Throughout the myocardium there are small foci, the centre of which often consists of necrotic or hyaline material and around it large epithelioid cells with bulky vesicular nuclei and a more or less basophilic cytoplasm. Many of these cells contain several nuclei and are apparently identical with the Aschoff cells of rheumatic fever. In these nodules there also is some fibroblast proliferation and infiltration with lymphocytes, plasma cells and polymorphonuclear leucocytes. The nodules are evidently the experimental counterpart of Aschoff bodies (Figs. 9 and 11). In contrast to these obviously proliferative nodules, we note, in other parts of the myocardium, replacement of degenerating muscle fibres by ordinary, sometimes œdematous, connective tissue (Fig. 8). These non-specific foci are apparently identical with those seen by Darrow and Miller.[28]

In some of our animals, we also noted lesions resembling rheumatic endocarditis. As in the early stages of the spontaneous disease, the subendothelial layer is more severely affected than the endothelium itself. The lesion is also clearly proliferative. The nodules are very vascular and densely infiltrated by lymphocytes. There is marked proliferation of fibroblasts and Aschoff cells. In our animals the endocardium covering the papillary muscles was markedly affected (Fig. 10).

The histological changes in the pancreas result from similar vascular lesions. In the acute stages there is a great deal of œdema, while in more advanced cases, not only the blood vessels, but extensive portions of the connective tissue framework are transformed into hyalinized scar-like tissue (Figs. 12 and 13). Many of the Langerhans islets are likewise involved in this process of hyalinization, as are some of the pancreatic nerves. The latter are occasionally surrounded or infiltrated by leucocytes, thus exhibiting the picture of a neuritis.

The kidney shows a rather malignant nephrosclerosis as described in our previous publications. There is an enlargement, and often hyalinization, of the renal corpuscles, transudation of hyaline material into the capsular space and dilatation of the convoluted tubules many of which contain hyaline casts. The blood vessels, especially the medium sized arteries and arterioles, show the histological picture as described above for the mesenteric vessels. The structural similarity with the lesions of the mesenteric periarteritis nodosa and of the changes in the renal vessels in typical malignant nephrosclerosis are worthy of special emphasis. Some of the renal vessels are partially or completely thrombosed. This may be responsible for the occasional appearance of wedge-shaped infarct-like areas of dense sclerosis (Figs. 14, 15 and 16).

DISCUSSION

These investigations demonstrate the possibility of producing, with a corticoid hormone, nephrosclerosis with hypertension, as well as lesions similar to those seen in periarteritis nodosa, thromboangiitis obliterans and the rheumatic fever of human pathology. This makes it very probable that the above-mentioned diseases are closely related to each other. It is well known that exposure to sudden stress (toxic drugs, cold, acute infections, etc.) elicits an "alarm reaction" and if the damaging stimulus continues to act, this is followed by the resistant stage and eventually by the exhaustion stage of the so-called "general adaptation syndrome".[29] During this adaptation syndrome the adrenal cortex increases in size and produces excessive amounts of corticoid hormones. The symptoms and signs of the adaptation syndrome, and more particularly the response of the adrenal cortex, are comparatively independent of the specific nature of the eliciting agent and determined primarily by the intensity of the damage. One of the most prominent features of the syndrome is a break-down of body proteins. Conversely, exogenous administration of protein is preeminently capable of eliciting the syndrome and particularly the adrenal cortical stimulation. It is also known that corticoids increase general resistance and facilitate adaptation to diverse damaging agents.[29]

These facts suggest, in conjunction with the observations described in this communication, that an increase of corticoid production, though advantageous for resistance to stress may elicit manifold pathological manifestations of corticoid hormone overdosage. The fact that such overdosage phenomena may be produced by endogenous corticoids is rendered highly

probable by other experiments as well. It has been found that exposure to cold, or other damaging agents causes rats, sensitized by salt treatment, unilateral nephrectomy, or preferably both, to develop pathological changes identical with those produced by D.C.A. administration (Selye, unpublished). Our interpretation of the above-mentioned facts may explain why acute infectious diseases (tonsillitis, scarlet fever, streptococcus infections) nervous shock, exposure to cold and other types of severe strain, so frequently precede the appearance of rheumatic fever, periarteritis nodosa and malignant nephrosclerosis. Hence, we believe that all these conditions are closely related to each other and should be regarded as diseases of adaptation. They are not the direct result of the apparent eliciting agent but are, at least partly, caused by an abnormal adaptive response of the adrenal cortex. We wish to emphasize, however, that this interpretation does not attempt to minimize the rôle played by microörganisms in the pathogenesis of these adaptative diseases. Infection may act, firstly, as a stimulator of adrenal activity, and, secondly, lesions produced by corticoids (*e.g.*, in the endocardium) may be sites of predilection for the localization of microbes. Thus, streptococcus viridans is certainly of great importance in subacute bacterial endocarditis, another disease frequently associated with a history of rheumatic fever.

Further experiments will have to show what circumstances determine whether the same agent will produce one or the other of the above-mentioned manifestations.

SUMMARY

Experiments in the rat indicate that the toxic effect of chronic desoxycorticosterone acetate overdosage are considerably increased by unilateral nephrectomy.

Severe overdosage with this corticoid reproduces in the rat morphological lesions similar to those seen in periarteritis nodosa, malignant hypertension and rheumatic fever.

It has been emphasized that in the human the development of these diseases is usually preceded by infections, exposure to cold or other damaging agents, and that in animals similar changes appear in the course of adaptation to cold and other noxious stimuli. Concurrently, during adaptation the adrenal cortex is increased in size and produces excessive amounts of corticoids. Hence, we believe that the above-mentioned diseases are, at least partly, caused by an abnormal (probably excessive) adaptive response of the adrenal cortex and represent diseases of adaptation.

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A statement on the keeping qualities of canned foods has been made by the Ministry of Food after consultation with the Ministry of Health, the periods during which the various foods may be stored applying to conditions obtaining in the ordinary home. Sweetened, full-cream condensed milk is best used within six to nine months, after which it tends to become sugary; whereas unsweetened condensed milk will keep for as long as three years. Canned fish and such meat packs as sausage meat, meat rolls, and galantines, tongues, and soup keep the best of all canned foods, and their "shelf life" extends to some five years. Honey and jams keep for at least three years if contained in lacquered tin plate cans, but if the ends of the cans are lacquered steel one year is the normal maximum life for jams. Vegetables in lacquered cans keep well for at least to years, but beans in tomato sauce will keep even longer. One year only may be regarded as the full "shelf life" for soft stone fruits, and they should be kept in a cool place.—*J. Roy. Inst. of Pub. Health & Hyg.*, 1943, **6**: 190.