TABLE I

Serial number	Name	Age	Operation	Period of follow-up	Result
1	S. R. ..	35	Partial excision with silk repair.	3½ years	Fair.
2	M.	42	Do.	2 „	Good.
3	L.	38	Do.	3 „	„
4	R. B. ..	40	Do.	3 „	„
5	Mrs. A. M. ..	45	Do.	3 „	„
6	H. C. M. ..	35	Do.	2 „ 10 months	„
7	M. D. ..	52	Partial excision with fascia lata repair.	3 „	Excellent.
8	M. L. M. ..	49	Do.	2½ „	Good.
9	M. R. ..	52	Do.	2½ „	„
10	A. C. D. ..	49	Do.	2 „	„
11	S. C. D. ..	36	Excision of upper fragment with fascia lata repair.	2 „	„
12	A. B. D. ..	40	Partial excision with fascia lata repair.	1 year 10 months	„
13	A. C. ..	29	Do.	1 „ 10 „	„
14	A. D. ..	48	Do.	1 „ 9 „	„
15	J.	39	Do.	1 „	Excellent.
16	S. D. G. ..	42	Do.	1 „	Good.
17	M. M. ..	36	Do.	9 months	„
18	K. L. M. ..	45	Suture with silk through drill holes.	8 „	Good but sinus persisting.
19	K. R. B. ..	58	Do.	6 „	Fair.
20	B. B. B. R. ..	68	Partial excision with fascia lata repair.	5 „	Excellent.
21	S. C. S. ..	40	Do.	5 „	„
22	A. L. D. G. ..	62	Do.	4 „	Fair.
23	Dr. P. C. S. ..	42	Do.	2 „	Good.

claim however is that where, as in the majority of cases, the line of fracture passes through or about the junction of articular and non-articular areas of the bone, this operation of partial excision with firm fascia lata repair of the aponeurosis produces results better than those we have hitherto obtained.

I must express my indebtedness to my Registrar Dr. S. Neogi in helping me with case records and follow-ups and to Drs. B. Sen and B. Sengupta for the photographs. I must also thank Dr. R. Roychowdhuri for his ready co-operation in taking the numerous *x*-rays that illustrate this paper.

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P.S.—Since this paper was completed, I have operated on a series of further 8 cases by the above method. The results have been 'good' to 'excellent'.

PRODUCTION OF EPIDEMIC DROPSY IN MONKEYS*

By N. K. CHAKRAVARTY
and
R. N. CHAUDHURI
(From the Epidemic Dropsy Enquiry, financed by the Indian Council of Medical Research, Department of Tropical Medicine, School of Tropical Medicine, Calcutta)

IT is now generally accepted that epidemic dropsy is caused by the ingestion of argemone oil, used as an adulterant of mustard oil.

*This formed part of an article entitled 'Observations on Epidemic Dropsy' read at the 38th session of the Indian Science Congress, Bangalore, January 1951.

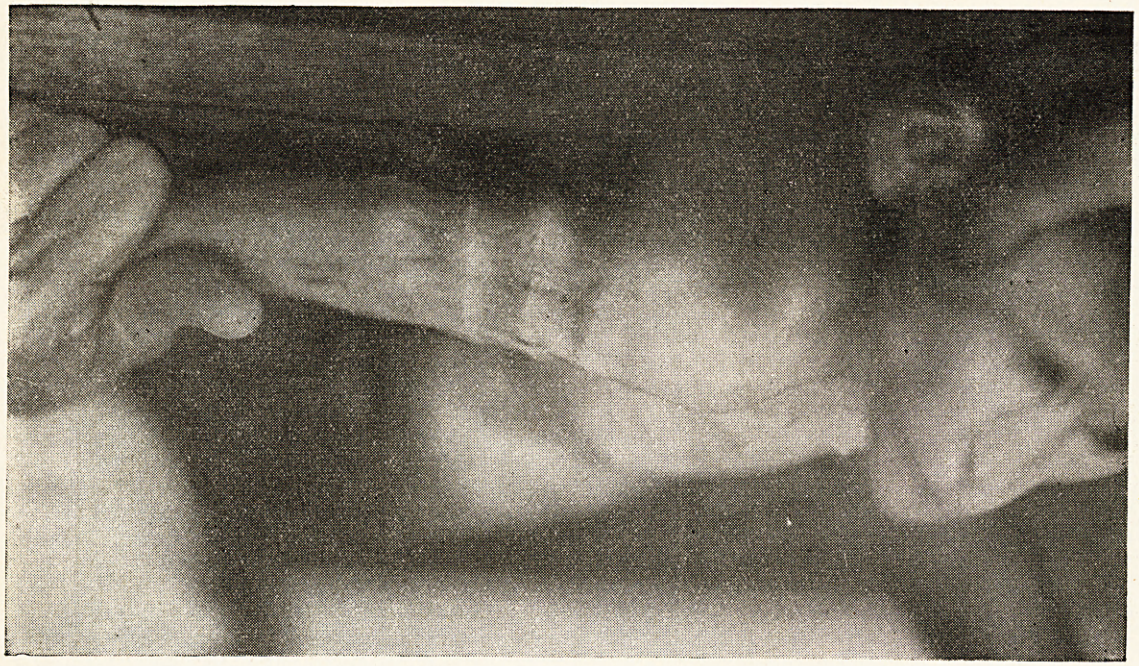
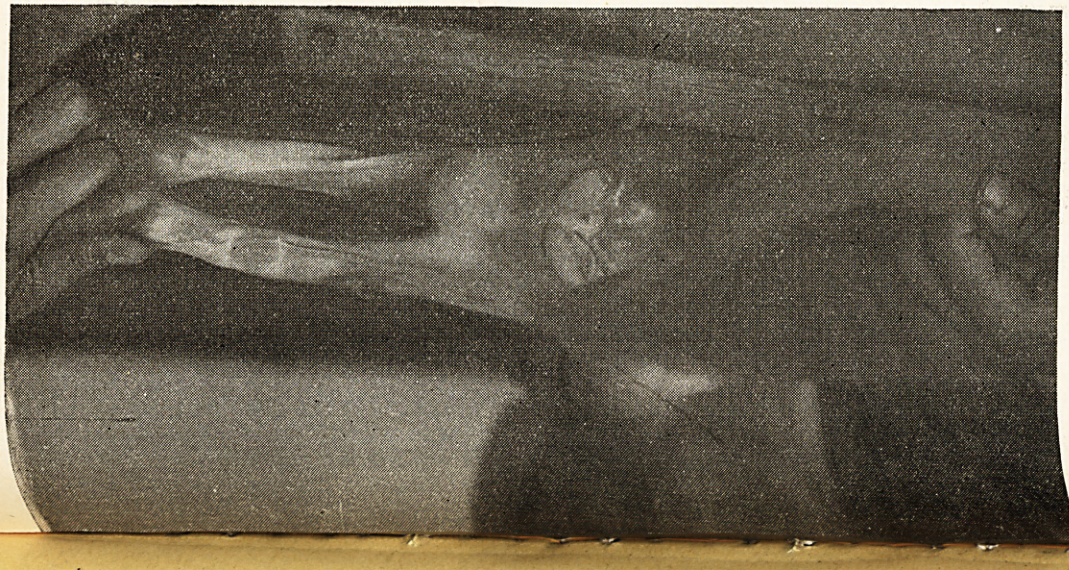


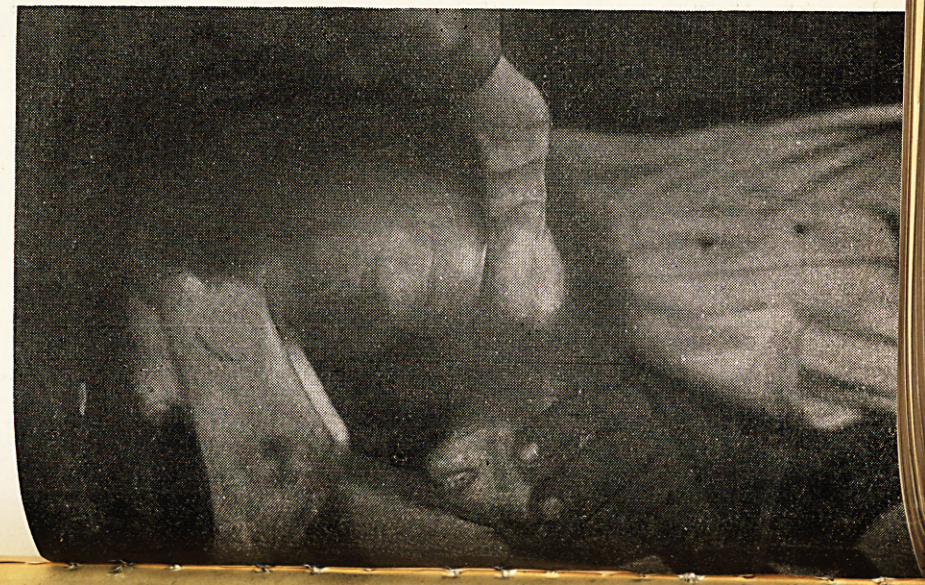
Fig. 1.

Fig. 2.

Fig. 3.

Fig. 4.





Besides epidemiological observations, the experiments on human volunteers by Lal and Roy (1937) and Chopra *et al.* (1939) lent further support to this theory, but the disease has not so far been reproduced in animals. We have, for some time past, started an experimental investigation into some of the still obscure problems of epidemic dropsy. The work that engaged our immediate attention was reproduction of the disease in animals and elucidation of the rôle of other factors, if any, in the causation of epidemic dropsy. Our preliminary observations on the first of these two aspects of the problem have been reported in the Report of the Scientific Advisory Board, I.C.M.R., 1950, and are presented in the following pages.

Argemone oil was administered by stomach tube, by intramuscular injection and as inunction to several rhesus monkeys with or without alteration in the diet. Signs of epidemic dropsy in the form of œdema and erythema were clearly demonstrated in two of them, while a third animal painted with argemone oil developed erythema and reddish raised spots resembling nodules. The details of treatment and findings of these three animals are presented below :

Experiments

I. Female monkey—Weight : 6 lb., diet : rice. 25 per cent argemone oil in liquid paraffin ½ to 1 ml. per lb. used for feeding.

1 to 3 weeks—Rice diet only.

4 to 7 weeks—Rice plus 3 ml. oil daily for 22 feeds.

8 to 11 weeks—Rice plus 6 ml. oil daily for 22 feeds. Salt was added in the 11th week. Œdema 10th week +, 11th week ++, diarrhœa +. Weight : 9th week 4 lb., 10th-11th week 4½ lb., 12th week—animal died.

In the 10th week, the animal developed definite pitting œdema and later diarrhœa. The occurrence of œdema was confirmed by thiocyanate space estimation which was significantly high, *viz*, 435 ml. per kg. body weight.* There was slight cutaneous flush. The total plasma protein, albumin and globulin at this stage were 6.46 per cent, 3.6 per cent and 2.86 per cent respectively. In the eleventh week the pitting became more marked and a distinct swelling appeared in the perineal region (*vide* plate XXVII, figures 3 and 4).

Post mortem. Straw-coloured fluid was present in small amount in the abdomen and other serous sacs. The heart, lungs, liver, spleen, kidneys and meninges were congested. The total amount of oil administered to this animal was 198 ml. containing 49.5 ml. of argemone oil.

II. Male monkey—Weight : 6 lb., diet : normal.

Pure argemone oil sterilized by heating in boiling water-bath for an hour used for intramuscular injection.

1st month—6 injections = 6 ml.

2nd month—6 injections = 6 ml.—End of 2nd month—œdema +, flush +, weight reduced to 4¾ lb., later 5 lb.

3rd month—5 injections = 5 ml.—Œdema ++, erythema more marked.

4th month—2 injections = 2 ml.

The total amount, of oil administered was 19 ml. in the course of 3½ months after which the animal died.

The injections were locally irritant and had to be divided in 2 or 3 sites. The usual interval between the injections was 3, 4 or 5 days but was increased sometimes to keep the animal alive. Pitting œdema and cutaneous erythema blanching on pressure were first observed 2 months after the commencement of injections when 12 ml. of the oil were administered (*vide* plate XXVII, figure 1). The œdema was seen in the limbs and perineum and erythema in the limbs and face. The thiocyanate space was now 370 ml. per kg. (higher than normal) and after another 3 weeks 437 ml. per kg. when pitting œdema became more marked and abdominal veins were distended (*vide* plate XXVII, figure 2). The blood count after 2 months showed some normocytic anæmia : Hæmoglobin 9.07 gm. per cent (66 per cent Hellige), R.B.C. 3.22 million per c.mm., W.B.C. 28,000 per c.mm., poly. 48 per cent, lympho. 48 per cent, mono. 3 per cent, eosino. 1 per cent, E.S.R. 25 (Wintrobe). The blood chemistry was as follows : Total plasma protein 7.5 per cent, albumin 4.1 per cent, globulin 3.4 per cent, sugar 96 mg. per cent, N.P.N. 30 mg. per cent, uric acid 1.6 mg. per cent, creatinine 1.1 mg. per cent, serum calcium 9.2 mg. per cent, plasma chloride 606 mg. per cent (as NaCl).

Post mortem. Heart, lungs, liver, spleen, kidneys, adrenal glands and meninges were extremely congested. The liver and right ventricle of heart were enlarged. Serous fluid was present in the peritoneal, pleural and pericardial cavities.

III. Male monkey—Weight : 5¾ lb., diet : normal.

Argemone oil, 1 ml. painted on shaved abdomen by 25 applications (25 ml.) in the course of a month.

1st, 2nd and 3rd weeks—no signs.

4th week—erythema on painted areas. No œdema. Reddish circumscribed raised spots. Died at the end of 4th week.

* The average thiocyanate space in 12 control monkeys was found to be 275.25 ml. per kg., the range being 240 to 333 ml. per kg.

Post mortem. Congestion of liver, kidneys, heart, lungs and meninges.

Histological changes

The histological changes simulated that of epidemic dropsy and were similar in all the three monkeys, though somewhat more marked in the injected animal (*vide* plates XXVIII to XXXI, photomicrographs 1 to 14). The changes were as follows :

Heart.—Dilated vessels separating the muscle fibres.

Lungs.—Congestion and in some exudation of fluid and red cells into the alveoli.

Skin.—Many dilated blood vessels in the dermis and subcutaneous tissue.

Liver.—Marked congestion of the central veins and sinusoids separating liver cells and fatty infiltration in some animals.

Kidneys.—Congestion of blood vessels and glomerular tufts.

Spleen and lymph glands.—Congested or normal.

Intestine.—Congested or normal.

Adrenal cortex.—Dilated capillaries separating the parenchyma cells.

Brain.—Meninges congested; dilated vessels were sometimes seen in the brain substance, choroid plexus often congested.

Eye.—Dilated vessels in the choroid layer.

Discussion

Figures 1 to 4, plate XXVII, clearly demonstrate the œdema in two of the monkeys. The occurrence of œdema was confirmed by a rise in the thiocyanate space as reported above. Cutaneous erythema blanching on pressure was more pronounced in the injected monkey than in the orally fed animal and bouts of diarrhœa had appeared in the latter. It is evident from the data given above that argemone oil when administered to monkeys by injection with ordinary diet or by stomach tube with rice diet can reproduce some of the predominant signs of epidemic dropsy. The exact rôle of rice diet in the production of the disease cannot be definitely stated now. In the animal fed with rice and argemone oil the plasma proteins were not appreciably reduced. Besides, a control monkey was kept on rice diet alone (with salt in the later part) for 71 days at the end of which no œdema was observed and the thiocyanate space estimated on the 65th day was found to be normal. So, it appears that rice diet alone cannot cause œdema within the period stated. Subsequently we have carried out argemone feeding experiments on two groups of monkeys kept on ordinary and rice diet respectively. The rice-fed monkeys showed a greater tendency to accumulation of extracellular fluid in the form of ascites and hydrothorax, seen post-mortem.

The argemone oil injections were locally irritant and caused marked local swelling. The injections were given in the lower limbs leaving the upper extremity free for the demonstration of œdema and erythema. The distension of the abdominal veins in this animal appears to be due to intense engorgement of the hepatic vessels, probably causing some portal hypertension. The oil was administered to this animal by an unnatural route as it was thought that this might demonstrate the toxic properties more readily. The physical signs with post mortem and histological appearance of this animal resembling human epidemic dropsy made a sharp contrast to those of another monkey injected with pure mustard oil who developed no signs and no changes in the organs. So, after eliminating the possible fallacies with the help of control studies, there remains no doubt that these two monkeys represent the first successful reproduction of the disease in animals.

The third monkey was painted on the shaved skin with pure argemone oil. Besides generalized cutaneous erythema in the painted areas, some elevated spots had developed, and we thought this might develop into the nodules of epidemic dropsy if the animal lived longer. The histological picture (*vide* plate XXIX, photomicrograph 6), however, was not very suggestive of sarcoids. A lethal effect was produced in a month after 25 applications only and on post-mortem examination marked congestion of the internal organs was seen and histological studies revealed a picture similar to epidemic dropsy in man. These findings leave no doubt that the oil is locally irritant to the skin where it may produce general erythema and circumscribed lesions and it is absorbed through healthy skin producing systemic poisonous effect in the internal organs. Painting of argemone oil was later extended to more monkeys and the work so far accomplished confirms the initial observation that argemone oil is absorbed from the intact healthy skin. The implication of this finding in human epidemic dropsy is obvious. It may be presumed that such absorption also occurs in man. The similar local effect on human skin was noticed when one of the sweepers who used to hold the monkeys and had accidentally received a few brushes of oil on the back of the hands developed erythema blanching on pressure. Experiment on human volunteers with the object of finding out systemic effects after local application has not been undertaken but these animal experiments strongly suggest that such absorption does occur. Since it is a common practice to rub mustard oil on the skin, this may lead to the production of cutaneous and systemic manifestations of the disease.

The vascular congestion observed in the histological sections simulates the human disease. In epidemic dropsy the congestion is commonly

seen in the skin and subcutaneous tissues, ciliary body and subchoroidal connective tissue of the eyes, in the heart, lungs, liver, spleen, pia-arachnoid membrane, intestine, mesenteric lymph nodes, skeletal muscle, uterus and ovary. Congestion of adrenal medulla and a mild inflammatory reaction was seen in one case and separation of the cortical cells by œdema, in another. The kidneys showed congestion and œdema occasionally (Khan, 1880; Acton and Chopra, 1927; Shanks and De, 1931; De, 1933; De and Chatterjee, 1935; Tribedi and De, 1940). In the argemone-treated animals, we have observed vascular dilatation in the skin and subcutaneous tissues, heart, lungs, liver, kidneys, meninges and often in intestine, spleen and mesenteric lymph nodes. In the eye marked dilatation of vessels is more commonly seen in the choroid and subchoroidal connective tissue and only occasionally in the ciliary body. The argemone-treated animals show very constant changes in the adrenal glands. Both the cortex and the medulla are congested. The dilated capillaries in the cortex separate the parenchyma cells (*vide* plate XXX, photomicrograph 9). Vascular proliferation, a feature in epidemic dropsy, was, however, absent. In spite of this difference, the similarity is very striking both in the nature of the pathological change and in the selective affection of many structures, such as skin, eye and heart.

Conclusion

Epidemic dropsy has been produced in monkeys by administering argemone oil either by injection with normal diet or by stomach tube with rice diet. Argemone oil, when applied to the skin, produced local erythema and cutaneous lesions and changes in the internal organs showing that the oil is absorbed from intact healthy skin. All the three animals died of the toxic effects of argemone oil. The histological appearance of the tissues simulated that of human epidemic dropsy.

Our thanks are due to Dr. H. Chakravarti and Mr. P. Ghose for their help in this work.

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EXPLANATION OF PLATES XXVII TO XXXI

Figure 1.—Monkey injected with argemone oil a few days after œdema first appeared. Impression left by the fingers due to subcutaneous accumulation of fluid is shown in the picture.

Figure 2.—Monkey injected with argemone oil at the end of 3 months. More marked œdema is shown by finger impression.

Figure 3.—Monkey fed with 25 per cent argemone oil along with rice diet. The photo shows pitting below the right knee, swelling of perineum and finger impressions in right arm, all caused by œdema.

Figure 4.—Monkey fed with 25 per cent argemone oil along with rice diet. Œdema is demonstrated by the swelling of the perineum and finger impressions on the right leg; the diarrhœaic stools is also seen.

Photomicrograph 1.—Section of eye of a normal monkey for comparison. × 100. Note the blood vessels in the choroid layer.

Photomicrograph 2.—Monkey fed with 25 per cent argemone oil along with rice diet. Section of kidney showing congestion. × 50.

Photomicrograph 3.—Monkey fed with 25 per cent argemone oil along with rice diet. Section of liver showing marked congestion of the central vein and the sinusoids. × 225.

Photomicrograph 4.—Monkey painted on skin with argemone oil. Section of heart : The muscle fibres are separated by dilated and engorged capillaries. × 100.

Photomicrograph 5.—Monkey painted on skin with argemone oil. Section of liver shows fatty infiltration of hepatic cells and marked engorgement of the sinusoids. × 225.

Photomicrograph 6.—Monkey painted on skin with argemone oil. Section through a red nodular lesion of the skin : Œdema and congestion with keratinization and proliferation of prickle cell layer. × 100.

Photomicrograph 7.—Monkey painted on skin with argemone oil. Section through other portions of skin : Note the large number of dilated blood vessels. × 264.

Photomicrograph 8.—Monkey injected with argemone oil. Section of lung showing congestion of capillaries and exudation of fluid and red cells into the alveolar space. × 264.

Photomicrograph 9.—Monkey injected with argemone oil. Section of adrenal cortex : The cells are separated by dilated capillaries. × 264.

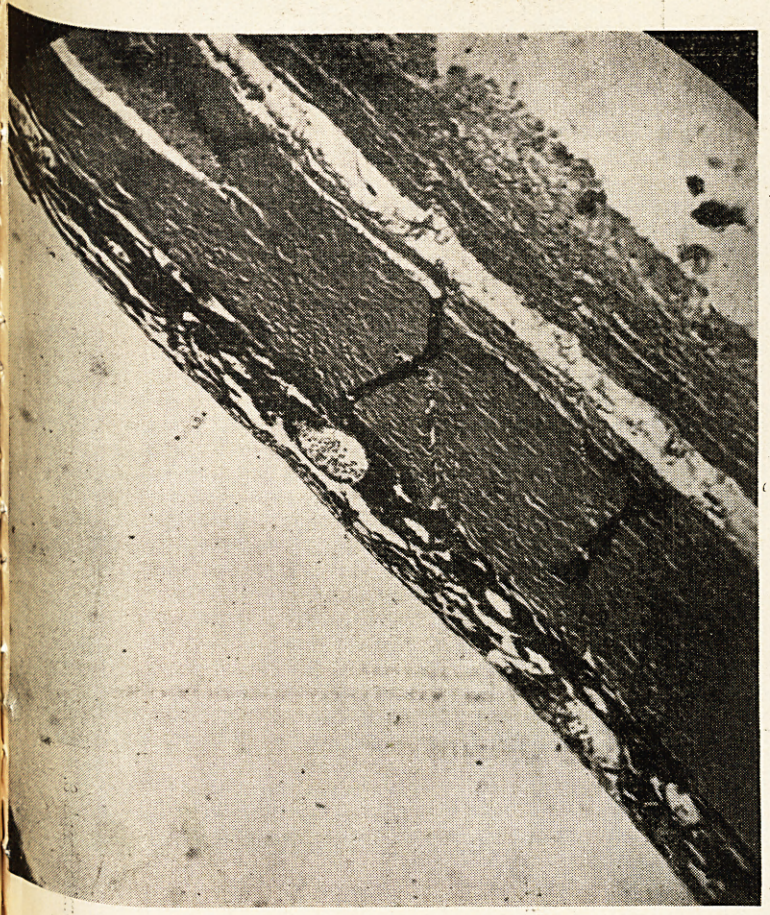
Photomicrograph 10.—Monkey injected with argemone oil. Section of eye through choroid layer : The choroidal vessels show intense dilatation and engorgement. × 100. Compare with photomicrograph 1.

Photomicrograph 11.—Monkey injected with argemone oil. Section of skin : Note the congested vessels in the dermis and subcutaneous tissues. × 100.

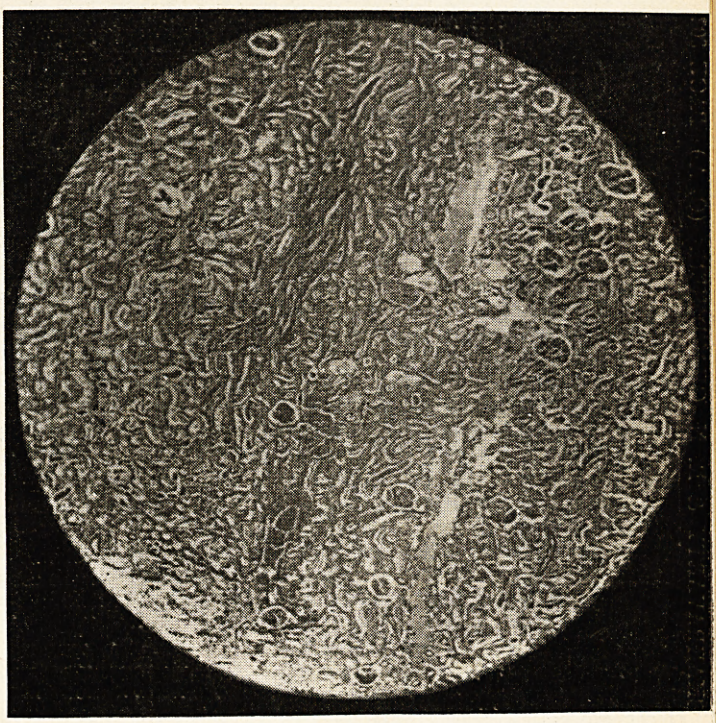
Photomicrograph 12.—Monkey injected with argemone oil. Section of liver : The hepatic cells are separated by wide areas of intensely dilated sinusoids. The kupffer cells are filled with pigments. × 215.

Photomicrograph 13.—Monkey injected with argemone oil. Section of intestine : Note the dilated blood vessels in the mucous membrane and submucous coat. × 100.

Photomicrograph 14.—Monkey injected with argemone oil. Section of heart showing marked dilatation of the capillaries with hæmorrhage separating muscle fibres. × 215.



Photomicrograph 1.



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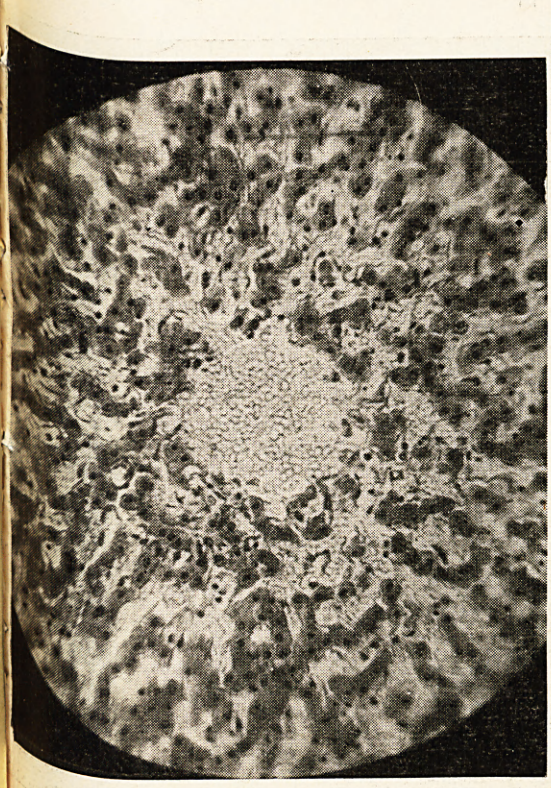

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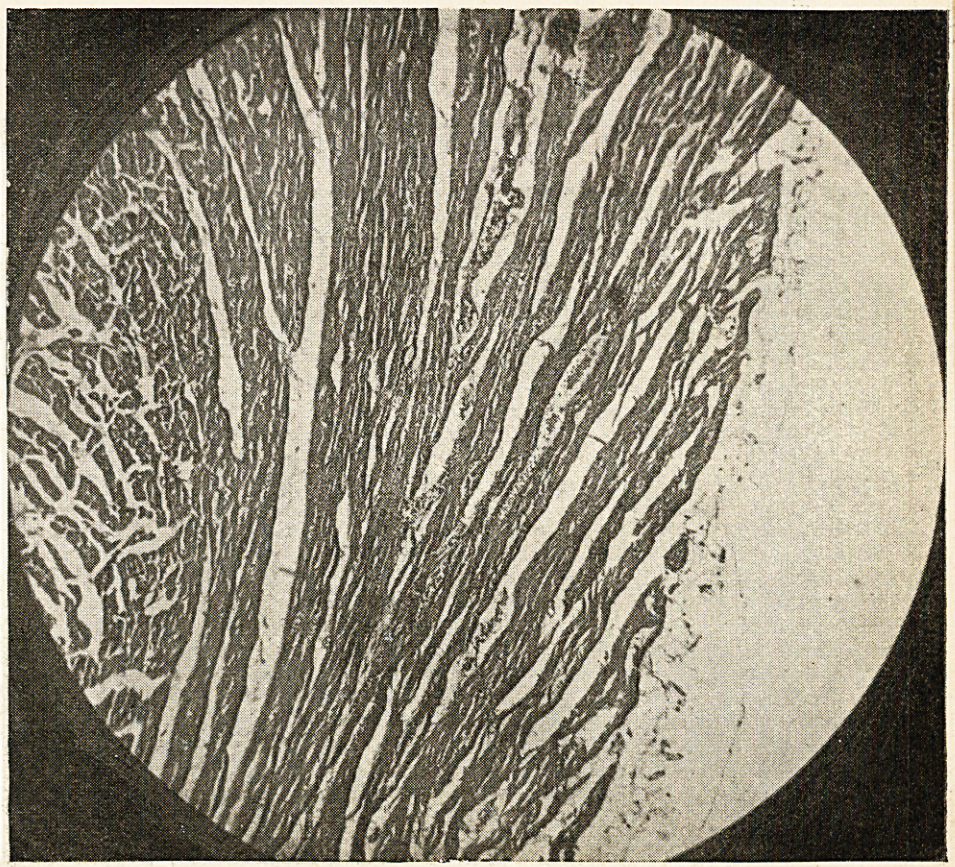

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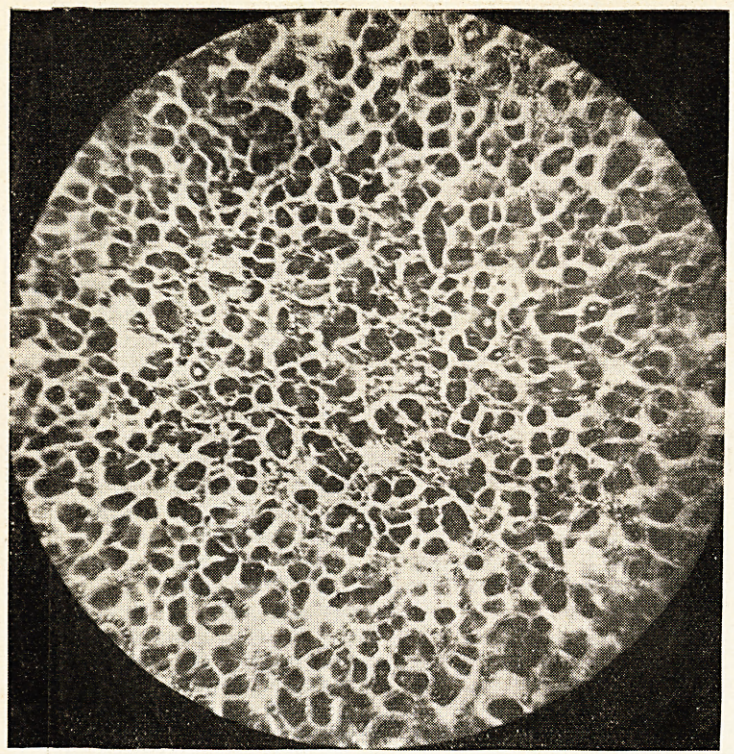
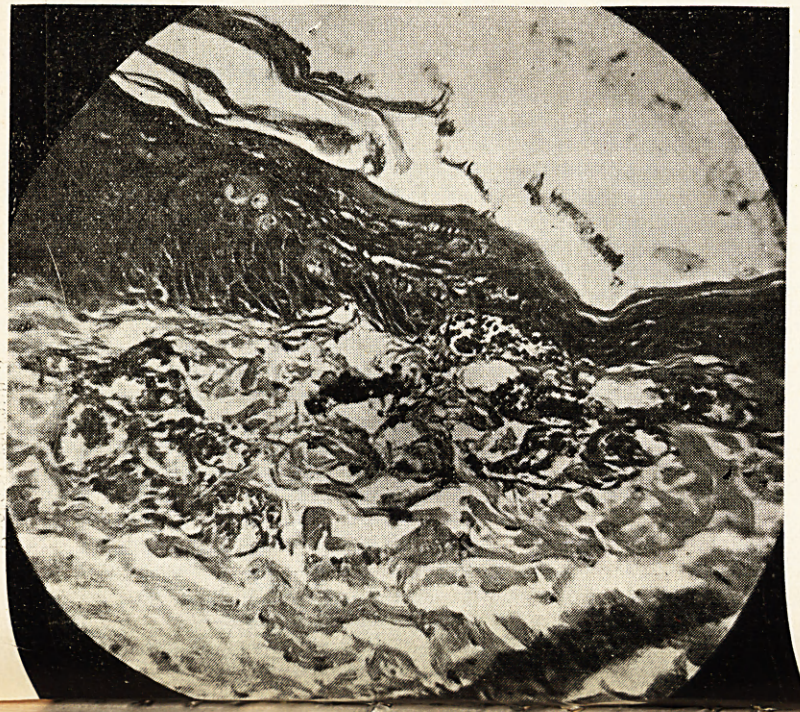
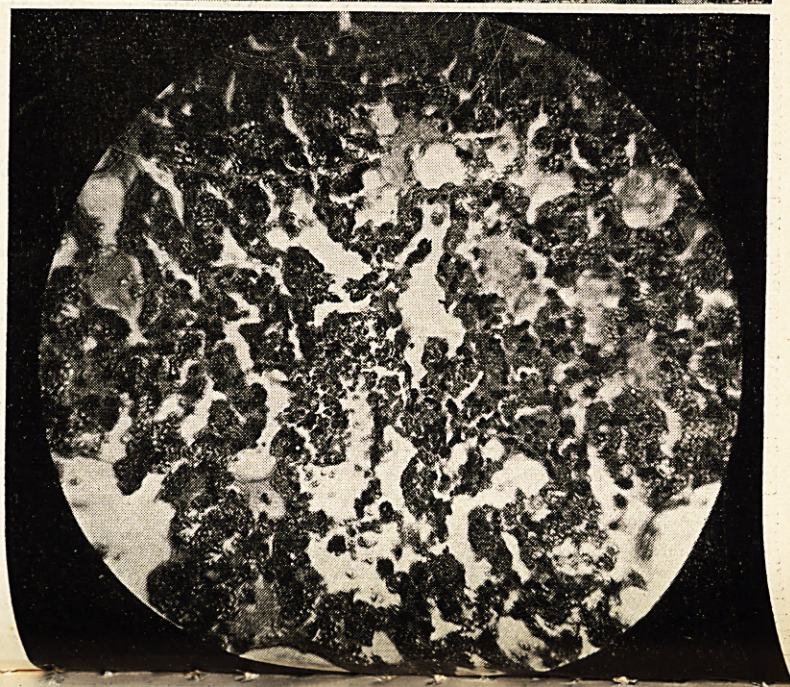


Photomicrograph 5.

Photomicrograph 6.



Photomicrograph 7.



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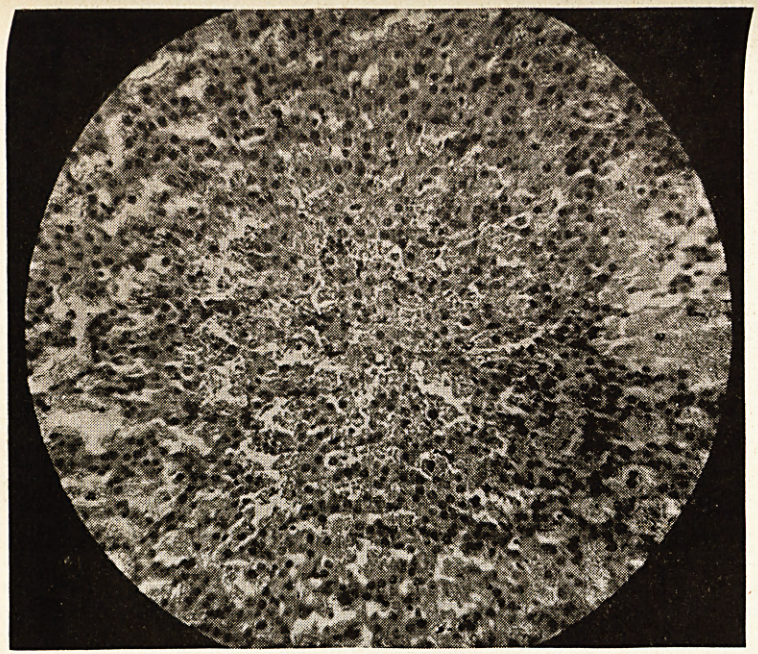


Photo-micrograph 9.

Photomicrograph 10.

Photomicrograph 11.

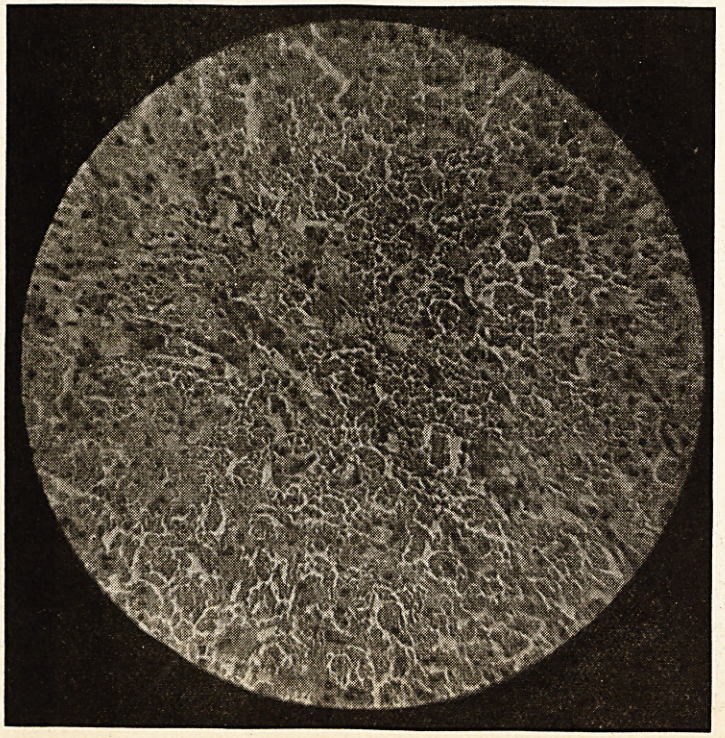


Photo-micrograph 12.

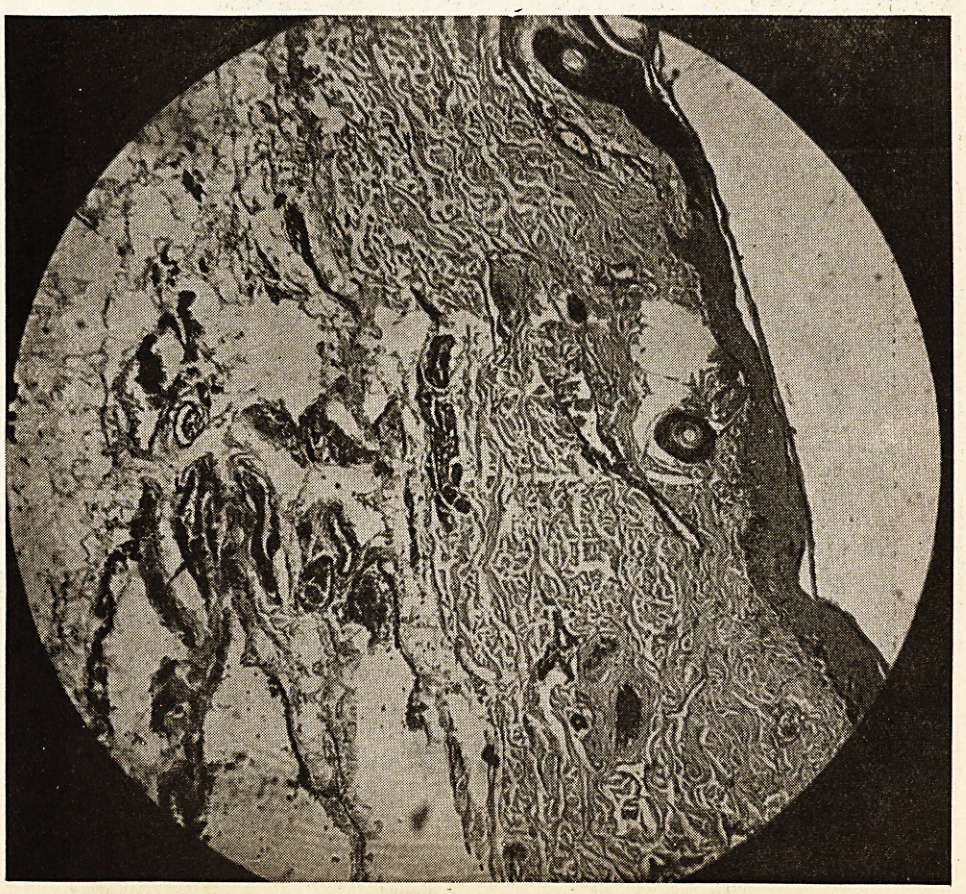
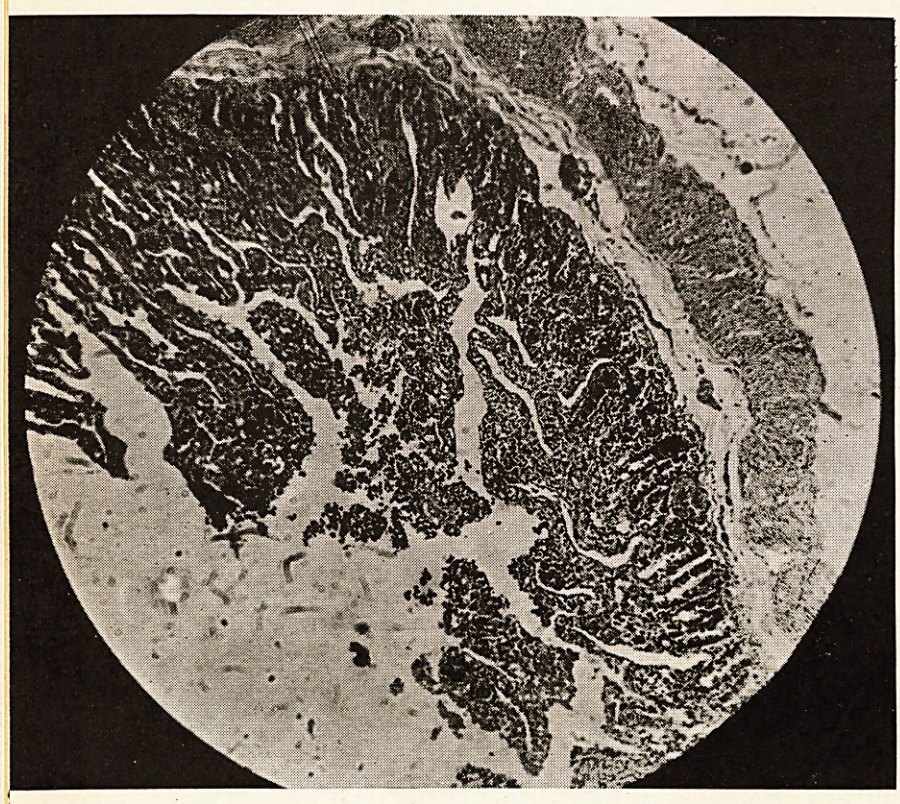


Plate XXXI

PRODUCTION OF EPIDEMIC DROPSY IN MONKEYS : N. K. CHAKRAVARTY & R. N. CHAUDHURI. (O. A.) PAGE 392



Photomicrograph 13.

Photomicrograph 14.

NOSE AND THROAT LESIONS IN CASES OF LEPROSY OF THE LEPROMATOUS TYPE : K. K. GHOSH, DHARMENDRA & N. C. DEY. (O. A.) PAGE 400

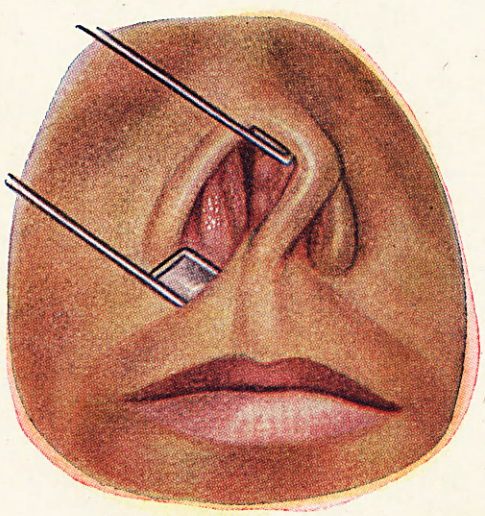


Fig. 1.

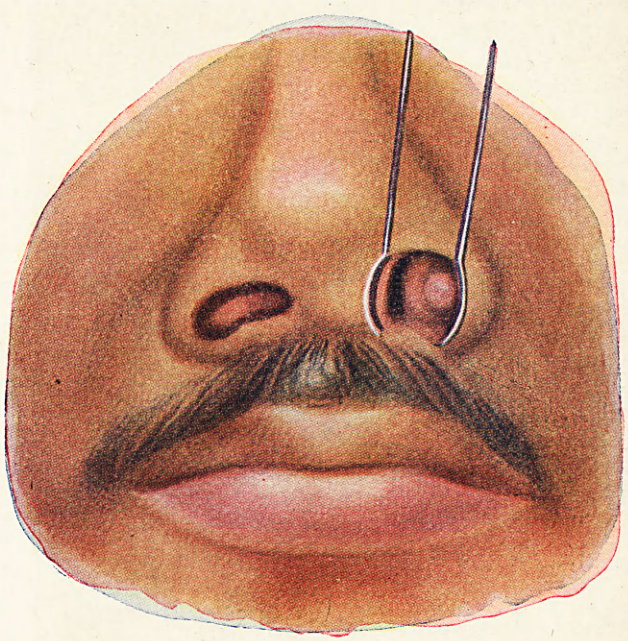


Fig. 2.