unchanged. Attempts to obtain solutions free from these small particles were without success, and accordingly we abandoned the use of analar phosphates in favour of the following preparation in which "specpure" Na_2CO_3 was dissolved in analar orthophosphoric acid. 0.29 g. of the "specpure" carbonate was dissolved in distilled water drawn direct from the still. To this 0.32 g. of analar orthophosphoric acid was slowly added and the solution made up to 100 ml., so giving a phosphate buffer of *p*H 7 containing 1 mg. P per ml.; 0.9 g. NaCl was then added The resulting solution was then refluxed and centrifuged as before. The degree of opalescence was less than in the previous case, and this procedure gave the cleanest buffered saline solution obtained.

The whole procedure was carried out in a still atmosphere as free from dust as possible. A measured small volume of phosphoric acid containing P^{32} was added to a suitable aliquot of the buffered saline solution in a clean ampoule, and the latter was then sealed and autoclaved as soon as possible. It is to be noted that the method of preparation described reduces the possibility of bacterial infection to a minimum while avoiding the rather serious complication of total aseptic conditions.

Results

The ampoule was opened and the β-particle activity of the uniformly mixed solution was compared with that of the supernatant solution after centrifuging at 2,500 r.p.m. for 20 minutes. This comparison was made with a standard "M6" liquid counter and also with differential β-particle ionization chambers, whereby the difference between the activity of the uniform solution and the supernatant was measured directly.

The results of tests on five different samples are tabulated below.

Sample No.	Ratio of Activity/ml. of Uniformly Mixed Solution to that of the Supernatant
X1	1·017
X2	1·015
+3	1·011
+4	1·012
+5	1·015

X, by counting technique. +, by ionization chambers.

It is concluded that the difference between the activity of the uniformly mixed solutions and the supernatant when the present procedure is carried out can be reduced to less than 2%.

It is not clear how far the results would be affected by changes in the carrier content of the solution. This important point is to be investigated.

The World Health Organization reports that the incidence of poliomyelitis was higher in Australia, the Belgian Congo, and the Netherlands than in the corresponding weeks in 1949 and 1950. In Switzerland, too, the incidence was higher; in the United States there were more cases than in 1950 but less than in the previous year. Austria, Canada, and the Western sectors of Berlin also had more cases than in the two preceding years. Scotland, Northern Ireland, and the German Federal Republic on the other hand reported fewer cases this year than in 1950 but more than in 1949; in France also the situation has improved since 1950, and England and Wales had fewer notifications than during the two preceding years.

SOME AUTORADIOGRAPHIC STUDIES OF NON-UNIFORM DISTRIBUTION OF RADIOACTIVE PHOSPHORUS IN TISSUES

BY

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[WITH SPECIAL PLATE]

For the purpose of estimating the dose of radiation received by tissues after the administration of radioactive isotopes, it is generally assumed that there is a uniform, or at least a continuous, distribution of isotope within a particular tissue or part of tissue considered. From the cellular point of view it is unlikely that this assumption will ever be justified, and even from the macroscopic view it is well known that the distribution of isotopes is often by no means uniform, as for instance in the case of iodine in the thyroid. There is clearly a need for a theoretical treatment of what might be called the "micro-dosimetry" of radioactive isotopes, but there is also need for further facts about the non-uniform distribution of isotopes in various tissues when administered in various ways, and for this reason the following observations on the non-uniform distribution of P^{32} in certain tissues are recorded.

Distribution of P^{32} in Rat Tissues Following Intravenous and Intraperitoneal Injection

It was found that certain autoradiographs of sections of rat liver and spleen following intravenous injection of P^{32} (as Na_2HPO_4) in normal saline prepared prior to the introduction of the special precautions described by Harrison and Raymond on page 930 showed by no means a uniform distribution of the isotope. This fact was first observed with contact autoradiographs of sections on *x*-ray film, and examples of such autoradiographs of rat-liver sections when the animals were killed at different times after injection (with 100 to 200 μc. of P^{32}) are shown in Figs. 1A, 2A, and 3A (Special Plate). Similar appearances on the autoradiographs were found in liver sections of rats sacrificed as long as three weeks after injection. The autoradiographs of spleen tissue also showed a similar "spotty" appearance, as did lung and bone marrow. Autoradiographs of other tissues did not show these local high concentrations of isotope. When, however, the injection was given intraperitoneally, no such spotty distribution of the isotope was evident. An example of an autoradiograph of a rat-liver section following intraperitoneal injection of the phosphate is given in Fig. 4.

Preparation of Tissues for Autoradiography

The fixative used for the tissues giving the autoradiographs of Figs. 1, 2, and 3 was 10% formaldehyde. 10-μ sections were cut, floated from water on to slides, and then clamped against "ilfex" *x*-ray film in a printing-frame for the required exposure time. Various investigations were carried out to ensure that the appearances in these autoradiographs were not artifacts.

Different fixatives were tried, including absolute alcohol and acetic alcohol, but in each case the same type of spotty appearance in liver and spleen was observed.

It was realized, of course, that in the normal methods of preparation of tissues for autoradiography much of the phosphorus, particularly that in the water-soluble form, is lost. Since this might possibly have some influence on the production of local concentrations an attempt was made to prepare sections for contact autoradiography with as little loss of P^{32} as possible. Various fixation techniques were tried, and in each case the liquids used in the preparation of the tissue blocks and sections were conserved and their activity measured by means of a liquid counter. Activity measurements were also made on weighed pieces of tissues adjacent to those used for blocking and sectioning so that the loss of activity could be determined as a percentage of the total activity present. In the case of liver and spleen, using 10% formaldehyde, it was found that 70% or more of the activity could be lost in the fixation procedures. However, if small pieces of tissue were taken and fixed rapidly in absolute alcohol (one or two hours) followed by xylol and embedded in paraffin wax, only 10% to 15% of the activity was lost. The sections were then cut and floated on warm mercury for transference to slides. Sections of rat liver prepared in this way gave contact autoradiographs showing the same type of spotty appearance as previously obtained, but with a higher background density than with the sections prepared in the normal way, as shown in Fig. 5.

Stripping Film Autoradiographs

Comparison of the contact autoradiographs of spleen and liver with the stained sections showed no apparent correspondence between the positions of the high concentrations and major vessels in the tissues. There also appeared to be no correspondence in position between concentrations shown on autoradiographs of serial sections. For further study of the location of the concentrations stripping film autoradiographs were made with the Kodak nuclear emulsion film NT2a, in stripping form, as described by Doniach and Pelc (1950), Berriman, Herz, and Stevens (1950), and others. After exposure and development the sections were stained through the film with haematoxylin. Figs. 1B, 2B, and 3B show the stripping film autoradiographs of sections from the blocks used for the corresponding contact autoradiographs. The stripping film autoradiograph in Fig. 3B had longer exposure than those in Figs. 1B and 2B. It is clear from these autoradiographs that the local concentrations of isotope occupy a very small volume. In most cases it was not possible to identify any particular histological structure underlying the concentrations because of the intensity of the blackening, but in certain cases the concentrations could be seen to coincide with the sinusoids of the liver.

Investigation of Human Tissue

Evidence has now been obtained that, following intravenous injection of P^{32} into a patient, the same type of non-uniform distribution can be found in the liver and spleen as was found in the rat tissues. A patient who had multiple secondaries arising from a shoulder sarcoma was given 5 mc. of P^{32} intravenously. He died, however, 17 days later, and it was possible to obtain pieces of liver, spleen, and secondary tumour for activity measurement and autoradiographic study. The activities of these tissues were found (using a liquid counter) to be : liver, 0.035 μc./g. ; spleen, 0.046 μc./g. ; secondary tumour, 0.029 μc./g.

Although these specific activities were very low compared with those in the rat studies, any high local concentrations of isotope might still be expected to show up on autoradiographs. 20-μ sections were cut and autoradiographs were taken with various techniques. Contact autoradiographs with x-ray film showed some evidence of local concentrations in the spleen. Through the courtesy of Dr. Herz, of Messrs. Kodak Ltd., it was possible to obtain x-ray emulsion in a stripping film. This could be applied to the section in the same way as the nuclear stripping film. The resolution obtainable was of course much below that of the thin nuclear emulsion, but was nevertheless much better than that obtained with ordinary contact autoradiographs on x-ray film.

Autoradiographs of the human spleen obtained with the x-ray stripping film showed that a number of highly localized concentrations were present, as can be seen in Fig. 6. In the liver a few concentrations were observed, but they were not so numerous as in the spleen. The sections of the secondary tumour showed no localized concentrations.

Source of the Concentrations

It is well known that if colloidal or particulate matter is introduced intravenously into an animal the particles will be taken up by cells of the reticulo-endothelial system, which will include the liver and spleen. The relative distribution in the various parts of the reticulo-endothelial system is believed to depend largely on the size of the particles (Dobson *et al.*, 1949). When, however, the material is given intraperitoneally the particles may be confined entirely to the peritoneal space and not be able to pass through the membrane into the various organs.

Thus the appearances found in the autoradiographs would be explained if the radioactive material of the injected solution was to some extent concentrated on particulate or colloidal matter, and in fact investigation has shown this to be the case. It does appear, however, that these concentrations of activity in the injected solution can arise at various stages, not only during the preparation of the active solution but also in manipulations preparatory to injecting it into the patient.

With the solutions used in the early part of these investigations the trouble was due mainly to particulate matter introduced in the course of preparation of the original solution. Contact autoradiographs of dried smears of the solutions as received, diluted in normal saline, gave clear evidence (Fig. 7*a*) of the presence of concentrations of activity. It was found with these solutions that their activity could be reduced an appreciable amount (up to 30%) by centrifuging (2,000 r.p.m. for 30 minutes). After intravenous injection of the supernatant solutions very few concentrations were observed in liver or spleen, while with the residual solution more concentrations were obtained than with the original solution. An example of this is shown in Fig. 7*b*.

As described by Harrison and Raymond, it has now been found possible to prepare the active solutions so that they behave as true solutions so far as various physical tests show. Active solutions prepared in this way were used in all the later autoradiographic studies

to be described, and in a number of cases there was no appearance of "spottiness" in the liver or other organs after intravenous injection. On other occasions, however, a spotty appearance was obtained, although not in general so marked as in the first series of experiments. Investigation has shown that this effect is again due to concentrations of activity in the injected solution which have been produced mainly in the syringe used for the injection.

Fig. 8A shows the result of an experiment in which the syringe was filled with enough active solution for two injections. The first injection was given after the solution had remained in the syringe for one minute, and only a slight spottiness is apparent in the liver autoradiograph. The second injection was given after one hour, and the spottiness in the liver is very evident. The increased spottiness after one hour might be due to the greater length of time for which the solution had remained in the syringe, but it could also be explained on the assumption that the concentrations are formed at the plunger end of the syringe, and that it is in the last injection, when the plunger is pushed right home, that the maximum spottiness is found. Tests made on a number of solutions have shown without doubt that the length of time for which the solution is left in the syringe is an important factor, but that the degree of spottiness obtained after a given time does vary considerably. The tests, however, have not eliminated the possibility of an effect arising at the plunger end of the syringe. In either case the development of the spottiness would be expected to depend on the precise state of cleanliness of the syringe, unless the concentrations are the result of some chemical action on the metal of the syringe. This possibility is to be looked into, but it may be noted that a spottiness has been found to develop in solutions in a syringe with a glass plunger. If the effects observed are the result of concentration of activity on particles present in the syringe, then a method of dealing with them would be to saturate the particles beforehand with inactive phosphate We have in fact found that by rinsing the syringe with 10% phosphate carrier before filling the spottiness can be reduced to very small proportions. In Fig. 8B is given an example of autoradiographs after intravenous injection from a syringe rinsed with phosphate carrier before filling. Even after one hour in the syringe very little spottiness is evident.

The method of using carrier to rinse out the syringe, and possibly other glassware used, before filling with the active solution, may well prove to be a valuable clinical procedure when solutions of high specific activity are used, and where the addition of a small amount of extra carrier is not contraindicated. We would like to thank Dr. L. H. Gray for the suggestion of rinsing out the glassware with carrier, which arose at a recent meeting* when the subject was being discussed.

The importance from the clinical point of view of the observations presented here is, first, that if a radioactive solution containing particulate or colloidal matter is administered to a patient the distribution of activity throughout the body will depend on the fraction of the activity concentrated on the particles, and also on the mode of administration. Secondly, in the tissues where the particles are held, the dose at and very near the concentrations may be very high compared with the mean dose throughout the tissue. It is clearly important to estimate so far as is possible the variation in dosage distribution that would occur with a degree of spottiness such as has been obtained in the experiments described here, and this is attempted in the next section.

*Meeting of the Hospital Physicists' Association at Southampton, March, 1951

Consideration of Dosage Distribution

The following is a calculation, made with a number of simplifying assumptions, to give some indication of how the dose will vary throughout a tissue if a beta emitter is disposed in the tissue in the form of localized sources of high concentration.

Consider a medium in which are distributed a number of radioactive sources each of strength M millicuries. Assume that, in tissue, the beta dose at a distance d from a small source is proportional to $\frac{e^{-\mu d}}{d^2}$ where μ is a constant, and that there are n sources per unit volume of tissue.

Let k be the dose (in a given time) at unit distance from a source of 1 mc. of the isotope considered.

Consider first the dose at a point P on the surface of one of the sources, assuming the source to be a sphere of radius a, within which there is a uniform volume distribution of isotope. The radius a is assumed small enough for absorption within the sphere itself to be neglected.

The dose at point P will be made up of two parts : (i) dose from the source itself $= D_i$; and (ii) dose from outside sources $= D_e$. Now, the dose at the surface of a small sphere uniformly loaded with the radioactive isotope, neglecting absorption, is

$$\tfrac{1}{2}\int_0^a \frac{k \times \rho \times 4\pi r^2 dr}{r^2} = 2\mu k \rho a$$

where ρ is the volume density of activity In the case considered $\rho = \frac{M}{4/3\pi a^3}$, so that $D_i = \frac{3Mk}{2a^2}$.

If n is large and the dimensions of the medium are large compared with the range of the beta particles, then the mean value of D_e can be taken as:

$$\int_{r=0}^{r=\infty} \frac{k \times \rho \times 4\pi r^2 dr}{r^2} \times e^{-\mu r}$$

$$= \frac{4\pi k \rho}{\mu}, \text{ where } \rho = nM.$$

Thus $$D_e = \frac{4\pi nMk}{\mu}.$$

The ratio α of the dose at the surface of the source to the mean dose throughout the irradiated volume will, if n is large, be given approximately by

$$\alpha = 1 + \frac{D_i}{D_e} = 1 + \frac{3}{8\pi} \times \frac{\mu}{na^2} \quad \ldots \quad (1)$$

In the more general case, the dose at the surface of a small spherical source of radius a and activity M_1, which is in a medium containing a number of other sources of average activity M, will be given approximately by

$$\frac{3M_1k}{2a^2} + \frac{4\pi n\bar{M}k}{\mu}$$

and $$\alpha = 1 + \frac{3}{8\mu} \times \frac{M_1}{\bar{M}} \times \frac{\mu}{na^2}$$

For the beta particles from P^{32} measurements (W. K. Sinclair, unpublished) have shown that μ has a value of the order of 7 $cm.^{-1}$, and therefore from equation (1)

$$\alpha = 1 + \frac{0{\cdot}84}{na^2}$$

Thus there will be considerable variation in the dose at various points in the tissue if $\frac{1}{na^2} \gg 1$—that is, if $n \ll \frac{1}{a^2}$.

For particles of radius 1 μ the dosage variation will be large if $n \ll 10^8$ particles per cm.[3]

The calculation so far given refers to the case when the whole of the activity in the tissue is in the form of concentrations. Let the activity which is uniformly distributed per unit volume of tissue be x times the activity per unit volume which is in the form of concentrations. It then follows that the ratio α is given by

$$\alpha = 1 + \frac{0{\cdot}84}{na^3(1+x)} \quad \ldots\ldots\ldots\ldots (2)$$

A Quantitative Estimation of the Dosage Variation

An estimate was made of n—that is, the number of concentrations per unit volume of tissue—from the contact autoradiographs of liver after intravenous injection of the solutions used originally, which contained particulate matter. In the cases studied the value of n was found to be of the order of 5×10^5. The average size of the particles involved is not known, but for the purposes of the calculation an average radius of 1 μ will be assumed.

Inserting these values in equation (2),

$$\alpha = 1 + \frac{0{\cdot}84}{5 \times 10^5 \times 10^{-8}(1+x)} = 1 + \frac{170}{1+x} \quad \ldots (3)$$

With the original radioactive phosphate solutions, in the worst case, centrifuging reduced the activity by about 30%. Thus about 30% of the activity was concentrated on particulate matter which could be centrifuged out. The liver and spleen will, however, take up a large part of the activity in particulate form, while the rest of the activity will be distributed throughout the body, and consequently in the case considered the activity in the liver in the form of concentrations may be 50% or more of the whole. Assuming that in the liver the activity in the form of concentrations is equal to that uniformly distributed, then $x=1$, and α has a value of the order of 100. With a lower value for n the value of the ratio α would be proportionately higher.

It is more difficult to estimate the fraction of the activity in particulate form when the concentrations have been produced in the syringe, since centrifuging cannot be carried out. However, the total activity of a weighed piece of the tissue used can be measured, and an estimate of the number of concentrations per unit volume made by counts on the autoradiographs. The value of n was found to vary between about 2×10^5 and 6×10^5 in five different experiments. An estimate of the average activity per concentration can then be made by grain counts on a stripping film autoradiograph of a tissue section. It has to be assumed, however, that no appreciable amount of activity is lost from the concentrations in the preparation of the tissue for sectioning and in the process of coating the section with the film. This is a serious assumption, for much of the uniformly distributed activity is known to be taken out by immersion of the tissue in water. However, an estimate obtained in this way would give a lower value for the activity in the form of concentrations. For the calculation it is necessary to know the appropriate grain yield for the Kodak stripping film. A series of experiments (unpublished) have been carried out, making stripping film autoradiographs of thin layers of gelatin containing a known amount of P^{32}. The photographic yield was found to be of the order of 0.7 developed grains per electron incident on the film.

The estimate has so far been carried out for one set of autoradiographs which showed quite marked spottiness in the liver after intravenous injection. The ratio of activity in concentrations to that uniformly distributed was calculated to be only about 1% in this case, leading to a value for the ratio α of only a little greater than unity. The true value, however, may be much higher than this, and it is hoped that it will be possible to make more reliable estimates once a technique has been perfected whereby all the activity in the tissue is retained throughout the autoradiographic process.

Clinical Significance of Presence of Particulate Matter in Administered Radioactive Solutions

The calculations given above indicate that, if a considerable fraction of the activity of the injected solution is concentrated on particulate matter, the dose received by the phagocytic cells engulfing the particles may be much greater than the average dose throughout the tissue. It should be noted, however, that a condition for a very high dose to these cells is that the number of particles per unit volume of tissue is relatively small, which implies that only relatively few of the phagocytic cells will receive the high dose.

The importance from the clinical point of view of the presence of the particulate matter in the administered solution must depend on the way in which the particulate matter is distributed throughout the reticulo-endothelial system. The studies of Jones, Wrobel, and Lyons (1944), using intravenous injection of chromic radioactive phosphate, indicate that the liver of the mouse and dog can withstand a very large dose. In some experiments the estimated average dose in the liver of the mouse due to the contained chromic phosphate was of the order of 80,000 r, with no obvious impairment of liver function. The same distribution of activity in the spleen, however, was found in some cases practically to eliminate the organ.

It is also evident that a localization of the active particles in the bone marrow could lead to serious effects. Dobson *et al.* (1949), using colloids of the radioactive rare earths, have obtained a high degree of localization in the bone marrow of animals when the particle size is small, but it is likely that there are considerable species differences and the results obtained with animals may not apply to man.

The contact autoradiographs given in Figs. 1A, 2A, and 3A indicate that the activity of the concentrations in the liver increases with time (from 15 minutes to 4½ hours after injection). This is unexpected, since the work of Dobson *et al.* (1949) with radioactive colloids has shown that the larger particles are removed first from the blood stream. There is, however, the possibility of a delayed transfer of particles from the lung to the liver and spleen, and it is hoped that it will be possible to investigate this in the near future.

The need for investigation of the effect of carrier content on the production of the concentrations of activity has been mentioned by Harrison and Raymond.

Summary

Autoradiographic studies have been made on rat tissue and also on a human post-mortem specimen after injection with active phosphate solution. The autoradiographs of the liver and of other tissues of the reticulo-endothelial system following intravenous injection showed a very "spotty" appearance. After intraperitoneal injection the distribution was found to be reasonably uniform. Autoradiographs of

smears of the original solution indicated that particulate material was present which concentrated the activity. This particulate material can arise in the preparation of the active solution but also, it has been shown, by allowing the solution to stand in a syringe, unless special precautions have been taken. The non-uniformity of activity resulting may affect considerably the dosage distribution in the tissue.

We wish to acknowledge our indebtedness to Dr. W. K. Sinclair, whose work first indicated the unsatisfactory nature of some of the radioactive solutions being used, to Miss H. E. Farran for her assistance in the activity measurements, and to Miss M. Winsborough for her help throughout the investigations. We are grateful for the help provided by Dr. Herz, of Messrs. Kodak, in the matter of autoradiographic emulsions. The co-operation of the staff of the Radiobiological Research Unit, A.E.R.E., Harwell, is gratefully acknowledged. Finally, we wish to express to Professor W. V. Mayneord our appreciation of the encouragement he has given us in this investigation.

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CHROMAFFIN TUMOUR WITH CHRONIC HYPERTENSION

BY

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[WITH SPECIAL PLATE]

The following case of a chromaffin tumour (paraganglioma) arising from the organ of Zuckerkandl is recorded in view of the extreme rarity of the tumour and also because of the well-marked clinical syndrome of apparent essential hypertension associated with it.

Different views have been held concerning which tumours should be grouped together under the heading of phaeochromocytoma, chromaffinoma, or paraganglioma. It is generally agreed, as pointed out by Hollingsworth (1946), that the ectoderm of the neural crest gives rise to the cells of the medullary part of the suprarenal gland, forming sympathoblasts which develop into ganglion cells, and phaeochromoblasts which develop into phaeochromocytes or chromaffin cells, distinguishable cytologically by the brown granules which form in their cytoplasm when treated with chromate solutions.

It is apparent that some of the phaeochrome cells become diverted from their course and, instead of taking part in the formation of the suprarenal medulla, become associated with pre-vertebral and peripheral sympathetic ganglia. It was to such cell masses that Kohn (1902) gave the title of paraganglia, the largest accumulation of which in the abdomen is formed by the organs of Zuckerkandl, situated along the aorta near the origin of the inferior mesenteric artery. Certain other tissue such as the carotid bodies, and the argentaffin cells in the bowel, have been linked with the paraganglia, but, as these structures have nothing in common embryologically, the association seems artificial.

It is common to employ the title "phaeochromocytoma" or "chromaffinoma" for those tumours arising from suprarenal medulla and to use the term "paraganglioma" for tumours arising from the extrasuprarenal chromaffin tissue.

Tumours arising from chromaffin tissue are very rare. Mackeith (1944) was able to discover only 152 cases in a review of the literature. Of these the vast majority arose from the medulla of the suprarenal gland, but a small number were found to have originated in other sites. Waaler (1945) reported 18 cases of extrasuprarenal chromaffin tumours in the literature, and of these 10 arose in the organ of Zuckerkandl (Stangl, 1903; Hausmann and Getzowa, 1922; Handschin, 1928; Nordmann and Lebkuchner, 1931; Merkulow, 1933; Cragg, 1934; Bauer and Leriche, 1934; Reichardt, 1934; Gellerstedt and Thyresson, 1939; Podloucky, 1940). The other cases were in a variety of situations in association with sympathetic elements in the abdomen. Two cases have been reported as arising from thoracic ganglia (Philips, 1940; Miller, 1924–5).

The clinical picture produced by these tumours appears to be caused by the secretion of adrenaline or an adrenaline-like substance into the blood stream, and four varieties of symptom complex are recognized. (1) Adrenal-sympathetic syndrome or paroxysmal hypertension, first described by Labbé *et al.* (1922) and more recently reviewed by Mackeith (1944) and Blacklock *et al.* (1947). (2) Persistent hypertension: a group of 51 such cases has been analysed by Green (1946). (3) Asymptomatic. (4) Malignant cases.

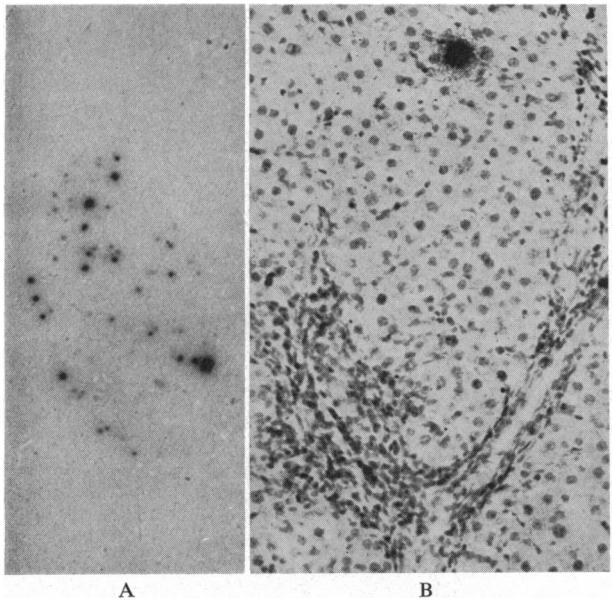
The following case falls into group 2 of the above classification.

Case Report

A woman aged 40 was seen in May, 1950, complaining of severe headaches. Since the age of 12 years she had suffered from attacks of headache lasting from two hours up to 48 hours. Onset was irregular and not associated with any "aura," with menstruation, or "bilious attacks." There were no visual disturbances. The most recent attack occurred one week before admission, following influenza, and was associated with nausea and vomiting. On this occasion the patient lost consciousness, which had never occurred before. She had no other neurological signs or symptoms. During the preceding five years she had noticed increasing dyspnoea and palpitations on exertion, and, while she had at one time been athletic, she had become unable to run upstairs. She had recently complained of easily becoming flushed in the face.

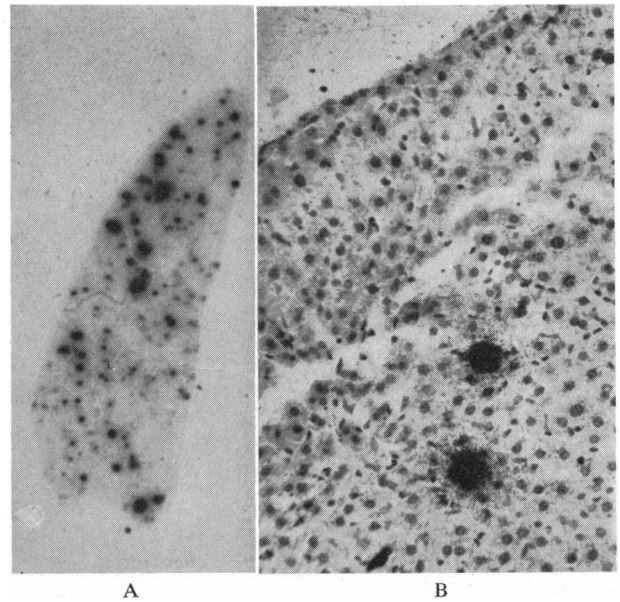
On examination and investigation no abnormalities were found except evidence of slight cardiac enlargement and accentuated aortic second sound. Electrocardiographic investigation showed a prominent P2 and displaced ST complex with flattened T wave in all four leads. The blood pressure, recorded on numerous occasions, varied between 230/130 and 180/130. It was thought that this patient had essential hypertension and that there was a recent exacerbation of her symptoms. There was no evidence of renal origin. The headaches had recently become incapacitating, and it was felt that, with the association of some recent sickness, this might be an atypical form of migraine. There was no evidence of vasomotor disturbance. At no time during her stay in the ward were there any marked variations in her blood pressure either when she was free of headache or when the headache was severe. The headache was not relieved by ergotamine tartrate, and the usual sedatives had very little effect. She was discharged to her home. It was felt that should her symptoms not improve sympathectomy might be justified.

In July, 1950, she was readmitted, and it was apparent that her condition had deteriorated. Headache was now



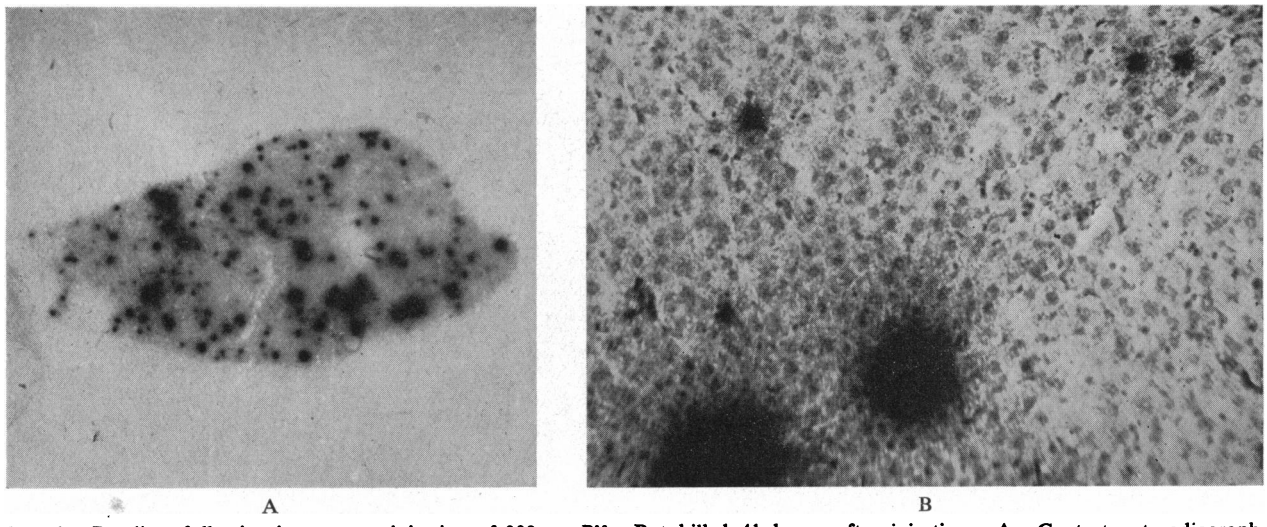
A B

FIG. 1.—Rat liver following intravenous injection of 300 μc. P^{32}. Rat killed 15 minutes after injection. A: Contact autoradiograph (*x*-ray film. ×5) B: Stripping film autoradiograph (Kodak nuclear emulsion stripping film). Exposure nine days. (×180.)



A B

FIG. 2.—Rat liver following intravenous injection of 300 μc. P^{32}. Rat killed 1½ hours after injection. A: Contact autoradiograph (*x*-ray film. ×5). B: Stripping film autoradiograph (Kodak nuclear emulsion stripping film). Exposure nine days. (×180.)



A B

FIG. 3.—Rat liver following intravenous injection of 300 μc. P^{32}. Rat killed 4½ hours after injection. A: Contact autoradiograph (*x*-ray film. ×5). B: Stripping film autoradiograph (Kodak nuclear emulsion stripping film). Exposure 39 days. (×180.)

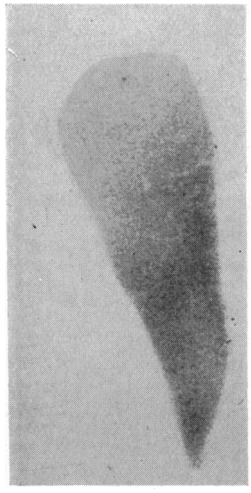
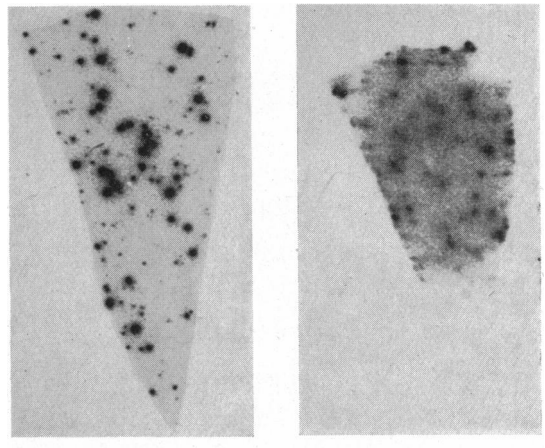


FIG. 4.—Contact autoradiograph of rat liver following intraperitoneal injection of P^{32}. (×5.)



Section floated out on water. Section floated out on mercury.

FIG. 5.—Contact autoradiographs of rat liver sections illustrating loss of P^{32} from section due to contact with water. (×5.)

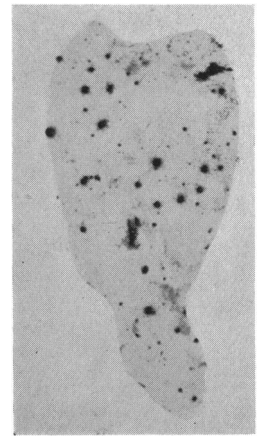


FIG. 6.—*X*-ray stripping film autoradiograph of piece of human spleen following intravenous injection of P^{32}. (×180.)

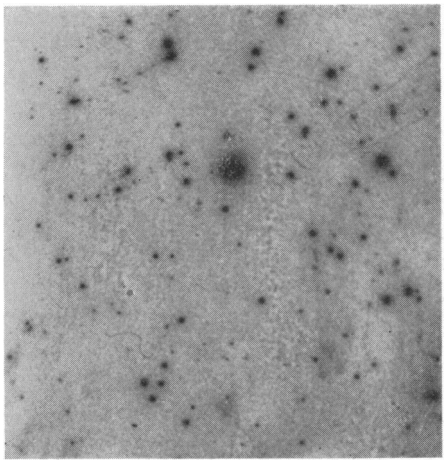
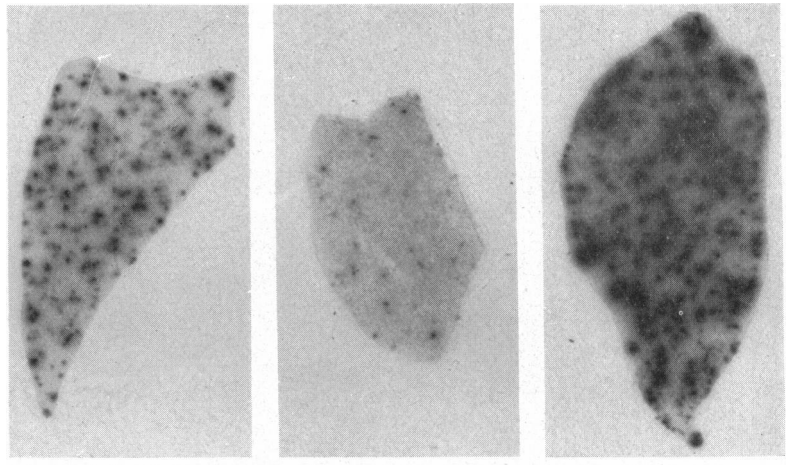
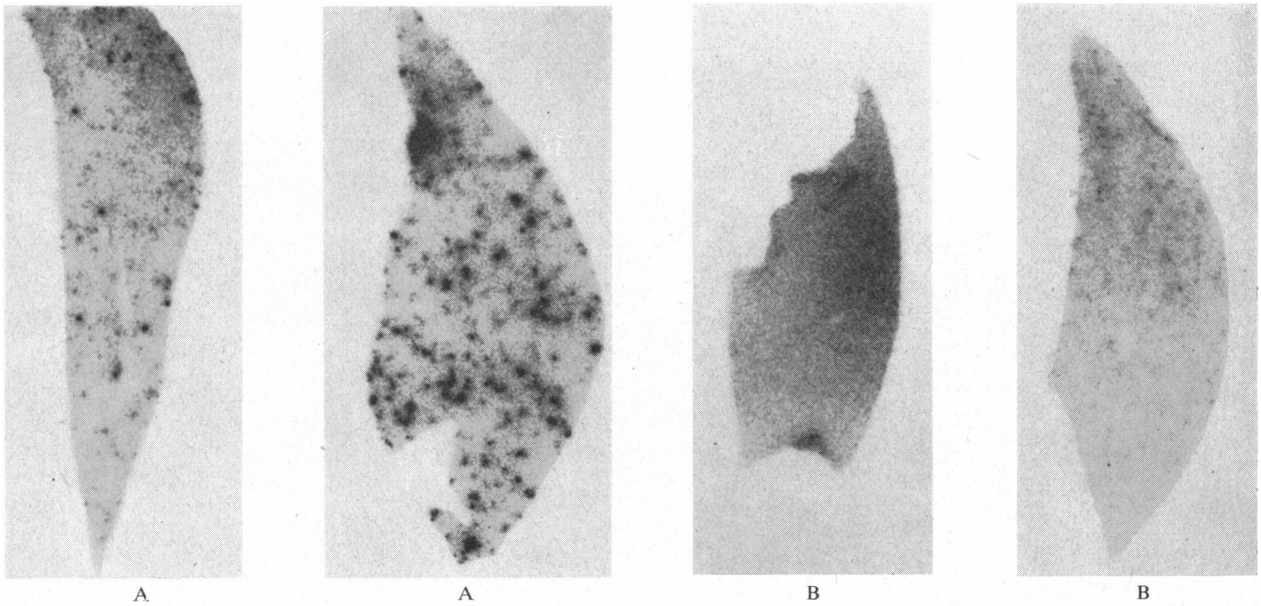


FIG. 7*a*.—Contact autoradiograph of smear of original solution of active phosphate. (×5.)



Solution before centrifuging. Supernatant solution. Residue.

FIG. 7*b*.—Contact autoradiographs of rat liver after intravenous injection with original solution, centrifuged solution, and residue. (×5.)



A Injection after 1 minute. A Injection after 1 hour. B Injection after 1 minute. B Injection after 1 hour.

FIG. 8.—Contact autoradiographs of rat liver after intravenous injection of active phosphate solution left in syringe for different lengths of time. (×5.) A: Syringe not rinsed out with carrier. B: Syringe rinsed out with phosphate carrier prior to filling.

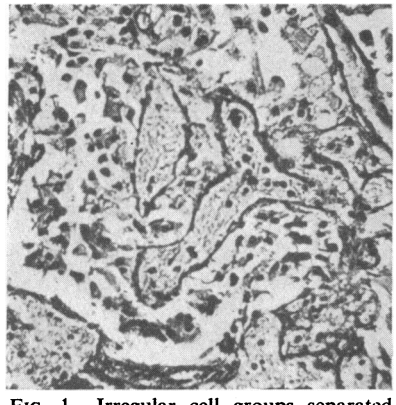


FIG. 1.—Irregular cell groups separated by thin-walled blood vessels. (H. and E. ×110.)

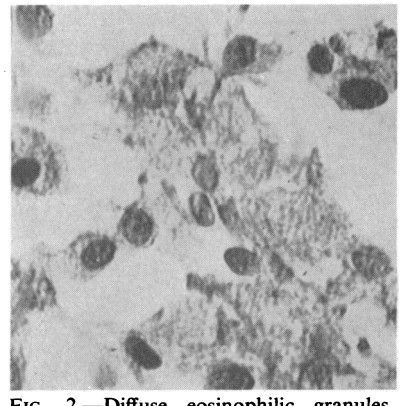


FIG. 2.—Diffuse eosinophilic granules. (H. and E. ×240.)

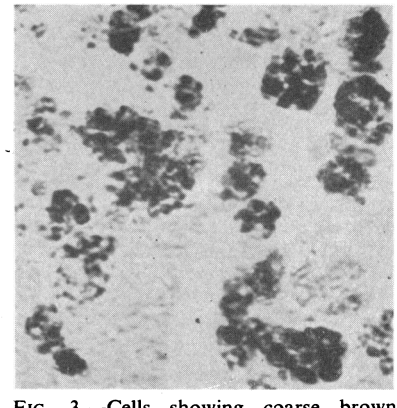


FIG. 3.—Cells showing coarse brown granules. (Ogata's silver impregnation method. ×240.)