radiotherapy, but it was applied as a routine to the scar whenever there was lymph-node invasion. In the unfavourable cases it did not, however, prevent local recurrence.

Conclusions

Radical thyroidectomy has limited indications. Its elective indication is papillary or pleomorphic orthoplastic cancer of slow evolution and with cervical lymphadenopathy. In such cases it is the operation of choice and gives the possibility of a ten-year cure without recurrence. Where recurrence follows a partial thyroidectomy the radical operation should still be attempted even if it is necessary to sacrifice the carotid artery or a nerve, as has sometimes happened in cases of recurrence of papillary cancer. It should be noted that, as in the case of other relatively slow-growing cancers, there may be a fresh local recurrence in the scar.

The indication for bilateral radical thyroidectomy seems to be a particularly clear one. The sudden suppression of thyroid function, in spite of compensatory medication, does not prevent metastasis or local recurrence. Where the operation has been aimed at inactivation of the metastases it has not been successful.

It is precisely to those forms of cancer which are already metastasizing but are still limited and growing slowly that this operation can be applied, leaving intact the healthy thyroid lobe, with complementary radiotherapy and with irradiation of any metastasis or, where possible, its removal. The results of such treatment are more encouraging than those of total thyroidectomy. *A posteriori*, it is true that with some anaplastic cancers or sarcomata it has proved useless. Punch biopsy of the thyroid gland is too risky, though it may be carried out tangentially where the tumour is large, but then only rarely. Where there is a definite sarcoma it is better to abstain from surgery altogether or to limit it to a partial operation in order to free the trachea or oesophagus, since in such cases radiotherapy is disappointing. But in other cases, even if radical thyroidectomy only serves as a palliative operation to free the respiratory and digestive tracts, it would still be worth while.

Only one point remains to be discussed: Should the operation be proposed as a matter of principle? *A priori*, the answer is No, since it would be necessary to confirm that every simple nodular goitre was malignant before dissection of the neck could be performed systematically. But when after a partial thyroidectomy for goitre it is learned that a cancer has been removed, early reoperation on the carotid sheath should be considered. Such an attitude does not often appear to be tenable, although the operation would certainly be of great value in such forms as papillary cancer. Even if it is carried out without delay after strumectomy it would still lose its character of an operation *en bloc*.

The psychological state of the patient must also be taken into account. A patient with cancer of the buccal cavity will more readily accept removal of affected lymph nodes as a matter of course, after radium treatment, than will a patient who has just been operated upon for what he had thought to be an ordinary goitre and who, a fortnight later, is asked to submit to another operation. That is why, on the whole, an expectant policy is more often adopted after subtotal thyroidectomy for early thyroid cancer. If during the operation examination by frozen section shows the existence of a

malignant lesion, a total extracapsular thyroidectomy with dissection of the recurrent laryngeal nerve should be carried out, but to subject a patient without warning to the mutilation following a block dissection of the neck is not to be advised. Here again it may be better to adopt a policy of "wait and see," particularly if probing of the carotid sheath with the finger reveals a suspicious nodule. But for the other varieties—lesions in the earliest stage, of the nodular type, operated upon for a simple goitre—this extensive prophylactic operation is not to be recommended.

BIBLIOGRAPHY

- Dargent, M. (1948). *Lancet*, 2, 721.
 — and Bérard, M. (1940). *J. Chir. (Paris)*, 55, 131.
 — and Berger, M. (1954). *Bull. Ass. franc. Cancer*, 41, 344.
 — and Guinet, P. (1952). *British Medical Journal*, 2, 1122.
 Frazell, E. L., and Foote, F. W. (1949). *J. clin. Endocrinol.*, 9, 1023.
 Joll, C. A. (1941). *Postgrad. med. J.*, 17, 166.
 Martin, H. (1954). *Cancer (N.Y.)*, 7, 1063.

DISSECTION OF AORTA AS A COMPLICATION OF TRANSLUMBAR AORTOGRAPHY

BY

H. GAYLIS, Ch.M., F.R.C.S.

AND

J. W. LAWS, M.B., F.F.R., M.R.C.P.

*From the Departments of Surgery and Radiodiagnosis, the
Hammersmith Hospital and Postgraduate
Medical School of London*

Percutaneous lumbar aortography introduced by dos Santos, Lamas, and Pereira Caldas in 1929 has become established as a procedure of proved value, particularly in the investigation of vascular and renal conditions. Complications, some fatal, were soon reported, and were partly responsible for the delayed acceptance of aortography in Great Britain and the United States of America. Although the nature of the contrast medium (100% sodium iodide) was responsible for some of the complications in the early cases, it was soon found that complications occurred even when less toxic substances were used.

Complications usually resulted from the injection of the whole or greater part of the contrast medium into a visceral branch of the aorta, resulting in damage to the organ supplied by the vessel, occasionally associated with thrombosis of the vessel itself. The more serious complications include gangrene of gut from superior or inferior mesenteric arterial thrombosis (Wagner and Price, 1950; dos Santo, 1955), anuria and renal necrosis from injection into renal arteries (dos Santos, 1955), hypertension with retinopathy (Miller, Wylie, and Hinman, 1954), acute pancreatitis from injection into the coeliac axis (Robinson, 1956), paraplegia (Boyarsky, 1954), rupture of the aortic wall (dos Santo, 1955), and chylothorax due to damage to the thoracic duct (Maluf and McCoy, 1955).

We wish to describe a complication—aortic dissection—in which a part or the whole of the contrast medium is injected into the media of the aorta causing a dissection (of the aorta) analogous to a spontaneous dissecting aneurysm and giving rise to a characteristic

radiographic picture. This complication is important for three reasons. It may give rise to misinterpretation in diagnosis if its true significance is not appreciated; there may be serious sequelae; and it may occur in spite of the most scrupulous technique. Furthermore, we believe that this event is not uncommon and that it offers an explanation for some of the complications of aortography usually ascribed to arterial thrombosis or to the direct toxic effect of the contrast medium.

Technique of Aortography

The technique of aortography, as used in the following cases, is described here, as it is relevant to the discussion.

Endotracheal general anaesthesia is used and the patient is placed prone on a simple cassette tunnel. A metal marker is placed on the skin over what is judged to be the spine of L1, and this is checked by a control radiograph. The aortography needle used is 16 s.w.g., 18 cm. long, and has a short bevel. A two-way tap, one opening of which is connected to a syringe containing heparin saline, and the other by means of "polythene" tubing to the syringe containing the contrast medium, is attached to the hilt of the needle. At a point about an inch (2.5 cm.) below the twelfth rib a nick is made in the skin to facilitate the introduction of the aortography needle. The needle is then inserted and directed upwards and medially towards the twelfth dorsal vertebra. After striking the vertebral body the needle is redirected in a more anterior plane until the aorta is encountered. The needle is then slowly advanced until a free reflux of blood enters the syringe containing heparin saline. No contrast injection is made unless this free reflux of blood continues after a trial injection of saline. The two-way tap is then turned so that the needle is connected to the contrast medium, when blood is seen to pulsate freely back along the transparent polythene tube. If this free reflux of blood continues it is assumed that the bevel of the needle is within the lumen, respirations are arrested by the anaesthetist, and the contrast medium is injected. In an adult approximately 30-40 ml. of 70% diiodone is injected in three to four seconds by a manually operated pressure pump. The first radiograph is exposed when two-thirds of the contrast medium has been injected, and four further films are taken in the subsequent 10 to 12 seconds by means of a simple hand-change cassette tunnel.

Case 1

A 58-year-old man was admitted to hospital complaining of pain in the right calf precipitated by walking a distance of half a mile and relieved by rest. The patient occasionally experienced coldness and tingling in the toes of the right foot. The symptoms had been present for a year and had become progressively worse. The past history was non-contributory.

Examination of Lower Extremities.—There were no obvious nutritional skin changes in the foot and no appreciable diminution of skin temperature. A systolic bruit was audible over the right external iliac artery immediately above the inguinal ligament.

Pulses	Right	Left
Femoral	Present but diminished ..	Present
Popliteal	Doubtful	Present
Posterior tibial ..	Absent	Present
Dorsalis pedis ..	Absent	Present

A clinical diagnosis of partial occlusion of the right iliac artery secondary to atherosclerosis was made.

A percutaneous lumbar aortogram showed a picture superficially resembling thrombosis of both common iliac arteries (Fig. 1). This was clearly incompatible with the clinical condition, since both femoral pulses were palpable, although the right was slightly diminished. In addition, it was noted that the radiographs showed no evidence of any significant collateral vessels—a feature so striking in a

complete thrombosis of the aorta (Fig. 2). We were forced to the conclusion that an intramural injection of contrast medium had given rise to this unusual radiographic picture.

FIG. 1.—Case 1. Aortogram showing complete arrest of the contrast medium at the bifurcation resembling bilateral common iliac thrombosis. Note the absence of collateral vessels. Compare with Fig. 2.

FIG. 2.—Case 1. Aortogram of a complete aortic thrombosis showing numerous collaterals. For comparison with Fig. 1.

Apart from severe backache which lasted for 24 hours there were no sequelae. There was no alteration in the peripheral pulses.

Case 2

A 62-year-old man was admitted to hospital complaining of severe pain in the right calf and thigh after walking a distance of 30 yards, which was relieved by rest. A year previously tenotomy of the right tendo Achillis had been performed with only temporary relief of pain. There were no obvious nutritional skin changes or muscle wasting in either limb. Systolic bruits were audible over both femoral and external iliac arteries, but were more pronounced on the right side.

Pulses	Right	Left
Femoral	Present	Present
Popliteal	Present	Present
Posterior tibial ..	Present	Present
Dorsalis pedis ..	Present	Present

A diagnosis of occlusive vascular disease of the iliac arteries was made.

The aortogram, which was performed without difficulty, appeared to show a complete thrombosis of the left common iliac artery with diffuse atherosclerotic changes involving the right common iliac artery (Fig. 3). Once again, however, this diagnosis was incompatible with the clinical features, since both femoral pulses were readily palpable both before and after aortography. There were no sequelae.

It seemed likely that, as in Case 1, the unusual appearances had been produced by some form of "extravasation," probably an intramural injection. This impression was strengthened as a result of examining a number of fresh human aortas, in which it was found that the wall of the aorta could be easily separated into two layers by gentle blunt dissection or intramural injection of saline. The plane of cleavage appeared to be adjacent to the intima.

FIG. 3.—Case 2. Aortogram showing non-filling of the left common iliac artery simulating thrombosis. Note the oblique translucent line across the contrast column near the tip of the needle and the double density near the origin of the right common iliac artery.

Experiment

In order to investigate the effects of intramural injection in more detail an experiment was designed to reproduce the conditions obtaining at aortography.

An abdominal aorta, including its bifurcation, was removed from a fresh cadaver and all its branches were ligated. This aorta was then incorporated into the circuit

FIG. 4.—Experimental aortogram (and diagram) showing the appearances following intramural injection. Note the non-filling of the left common iliac artery, simulating occlusion of the vessel, and the jet of contrast medium entering the right common iliac artery.

of the Melrose heart-lung machine (Melrose, 1953) and blood pumped through at the same rate and pressure as occurs in the normal abdominal aorta (approximately 3,000 ml. a minute, at a pressure of 100 mm. Hg). The aortography needle was introduced into the aorta, so that the bevel of the needle lay partly within the lumen and partly within the opposite wall of the aorta. At this stage blood returned freely from the hilt of the needle. Then 30 ml. of 70% diodone was injected rapidly in three seconds by means of the pressure injection apparatus, and serial films of the "aortogram" were taken by means of a simple hand-change cassette tunnel. The experiment was repeated on a number of aortas and radiographic appearance of various degrees of intramural dissection was demonstrated. The most interesting of these experiments demonstrated the passage of the contrast medium within the wall of the aorta from the point of the needle down to the bifurcation, giving an appearance of occlusion of the left common iliac artery (Fig. 4). This simulates exactly the appearance shown in the aortogram demonstrated in Fig. 3. A jet can be seen indicating where the contrast medium

FIG. 5.—Experimental aortogram taken 12 seconds after the injection, showing that most of the intramural contrast medium has been expelled into the lumen of the aorta. A little remains in the wall (→). The irregular calcification is due to atheromatous plaques.

has re-entered the true lumen of the right common iliac artery. A film taken 12 seconds after the injection showed that only a trace of contrast medium remained in the aortic wall, the rest having been squeezed out into the main lumen by the pulsatile flow of blood inside the aorta (Fig. 5).

FIG. 6.—Transverse section of aorta at point A on Fig. 4. Note a dissection in the media (→) extending for two-thirds of the circumference. Atheromatous plaque (↔).

FIG. 7.—Longitudinal section of aorta taken at point B on Fig. 4. Note the dissection in the media and the tear through the intima where the contrast medium has re-entered the lumen.

The aorta was then removed from the apparatus and fixed in formol-saline. Microscopy revealed that the dissection had taken place in the media, at the junction of the outer third and inner two-thirds (Fig. 6), extending two-thirds of the way round the circumference. The tear in the intima where the contrast medium had ruptured back into the main lumen of the right common iliac artery was clearly delineated (Fig. 7). These experiments reproduced and explained the unusual appearances shown in Figs. 1

and 3, and provided histological proof of the layer in which aortic dissection takes place. Furthermore, aortic dissection affords a probable explanation of a number of complications of aortography for which no very satisfactory explanation was previously available.

Discussion

Mechanism and Possible Effects of Aortic Dissection

Ideally, during percutaneous translumbar aortography the bevel of the aortography needle should lie completely within the lumen of the aorta prior to the injection of the contrast medium. If the bevel lies partly in the wall and partly in the lumen, injection of the contrast medium will cause aortic dissection. This undesirable position of the needle cannot readily be appreciated, because blood will still flow freely from the hilt of the needle in a pulsatile stream (Fig. 8 A). Occasionally only a little of the contrast medium enters the aortic wall (Fig. 8 B) and produces an appearance as in Fig. 9. Should larger quantities be injected intramurally a progressive dissection results and the origin of small blood vessels

may be torn (Figs. 8 C and 8 D). If these small arteries are lumbar or intercostal vessels ischaemia of the cord and paraplegia may result, in the same way as has been described by Weisman and Adams (1944) in spontaneous dissecting aneurysm of the abdominal aorta. Furthermore, if the bulk of the contrast medium is injected intramurally the aortic lumen may be temporarily occluded (Fig. 8 D) and give rise to an appearance simulating thrombosis (Figs. 1 and 3).

Another way in which a major branch of the aorta may be occluded is by an extension of the dissection into the vessel itself (Figs. 8 E, F, G). An example of dissection extending from the aorta into the renal artery is illustrated in Figs. 10 and 11. This aortogram was performed for the

FIG. 8.—Diagram to illustrate how faulty positioning of the aortography needle (A) may result in an intramural injection and dissection of the aorta (B). A progression of this dissection may result in the tearing of the origin of small branches (C) or the occlusion of the main aortic lumen (D). Occasionally the dissection may extend into and occlude a large branch of the aorta—e.g., a renal artery (F and G). N.B.: the bevel of the aortography needle has been deliberately exaggerated for clarity.

investigation of hypertension in a patient with a non-functioning left kidney on excretion pyelogram. There was a history of severe trauma to the left loin, with haematuria several years previously, followed by recurrent attacks of left loin pain. The non-filling of the left renal artery on the aortogram was explained when left nephrectomy revealed a hydronephrotic kidney with negligible renal substance and a small atrophic renal artery.

In the past, cases of gangrene of the bowel and renal necrosis have been ascribed to the local toxic effect of the contrast medium following the injection of the bulk of the

FIG. 9.—Aortogram showing minimal aortic dissection. A small quantity of contrast medium remains in the aortic wall at the tip of the aortography needle after the bulk has passed along the aorta and iliac arteries.

contrast medium into the vessel supplying the organ. This explanation is not an entirely satisfactory one, because there are numerous cases reported in the literature in which all the contrast medium has been injected into a single major branch of the aorta, such as coeliac, superior mesenteric, inferior mesenteric, or renal arteries, without any ill effects. It is more probable that in those cases in which complications have occurred part of the contrast medium

has entered the artery but simultaneous dissection has caused occlusion of the artery and stasis, thus allowing time for the concentrated contrast medium to exert its toxic effects on the organ.

Although we have been fortunate in that in our cases of aortic dissection there have been no serious sequelae, review of the literature reveals several reported cases in which it seems likely that dissection of the aorta has contributed to various serious complications.

Boyarsky (1954) described a case of complete motor and sensory loss below D 8 segment, occurring after aortography for demonstration of a possible aortic aneurysm. The aortogram was unsatisfactory, in that there was "uneven filling of the renal vessels, the aorta was not filled close to the point of insertion of the needle, but was outlined lower down, where it deviated to the left of the midline. The right iliac artery was filled, but the left was not," even though at clinical examination "there were no obliterative changes in the extremities." These clinical features closely resemble those described in Case 2. Boyarsky considered that the probable cause was thrombosis of the anterior spinal artery or direct toxic action of sodium acetrizolate on the cord. From the description of the aortogram, however, it seems probable that aortic dissection occurred similar in type and degree to our Case 2. Some small intercostal and lumbar arteries may well have been torn and the neighbouring spinal cord damaged by interference with its blood supply, in the same way as in a spontaneous dissecting aneurysm.

Antoni and Lindgren (1949) described a case of paraplegia and paresis of the bladder and rectum following aortography. This patient later developed gangrene of the right leg, and died three months after the aortogram. The aortogram was unsatisfactory, since "contrast injection showed that only a part of the aorta down to the superior border of L 2 and vessels in the upper abdomen, became contrast-filled. The point of the needle was at the height of the inferior border of L 1. A part of the contrast medium also proved to lie perivascularly." The following morning there was complete paralysis and anaesthesia from and including the dermatomes T 12 and L 1. At necropsy three months later, the cord was completely necrotic from and including the first lumbar segment, and there were both old and fresh thrombi in the right common iliac artery. The lower intercostal arteries were dissected and examined, but it was "impossible to observe any noteworthy alterations." The cord lesions were attributed to prolonged pressure on the abdominal aorta, due to the patient lying prone with an air pillow under the abdomen—supporting Steno's experiment (Niels Stenson, 1638–86), in which compression of the abdominal aorta at the level of the renal arteries in rabbits produced motor sensory paralysis of the lower part of the body. In view of the technically unsatisfactory aortogram with some contrast medium lying perivascularly, it seems more likely that damage to the cord resulted from aortic dissection and consequent interference with the blood supply of the spinal cord. Unfortunately there was no record of the microscopical appearance of the aorta or its branches.

Dos Santos (1955) quotes a case in which intra-adventitial injection of the whole dose of 100% sodium iodide (100 g. salt in 100 ml. of solution) was followed a week later by death due to rupture of the aortic wall. The radiograph showed an extravasation which outlined the contour of the aorta up to the thorax. By description this rupture may well have resulted from intramural injection causing medial dissection and a local necrosis of the aortic wall. Unfortunately microscopical confirmation is not available.

Smith, Rush, and Evans (1951) described a case in which contrast medium was injected into the wall of the aorta and the patient died 24 days later, owing to "cardiac failure from arteriosclerotic hypertensive disease." The published radiograph shows dissection extending along one renal artery into the base of the other. They state that at necropsy "the aortic wall and peri-aortic area were without abnormality," but it should be remembered that the necropsy

FIG. 10.—Aortogram showing dissection extending from the aorta along the right renal artery.

FIG. 11.—Aortogram taken five seconds after Fig. 10, showing retention of contrast medium in the dissection and persistent nephrogram probably due to stasis following partial occlusion of renal artery.

was carried out at least 24 days after the injection, and unfortunately there is no report of microscopical examination.

Miller, Wylie, and Hinman (1954) described a case in which aortography was followed by severe hypertension (B.P. 230/120) with retinopathy. Aortography revealed "peri-aortic extravasation" and direct injection into the right renal artery. An examination of their published radiograph, however, shows strong evidence of aortic dissection which extends into the left renal artery. The right renal artery is unfortunately obscured by the peri-aortic extravasation of contrast medium. Excretion urography showed a non-functioning right kidney, but six weeks later both kidneys gave normal urograms and the blood pressure had returned to the former normal level (140/90). The sudden development of hypertension in this case was presumably due to renal ischaemia, the result of dissection along a renal artery producing a Goldblatt type of renal lesion.

The difficulties of ensuring that the whole of the contrast medium is injected into the lumen has been commented on by many authors, some of whom have adopted other techniques. Fariñas (1941) exposed the femoral artery and passed a catheter up into the aorta. Peirce (1951) and Lindgren (1953) introduced a technique involving percutaneous puncture of the femoral artery with a trocar and cannula, through which a polythene catheter was passed. Seldinger (1953) devised the technique of catheter replacement of a trocar.

Concerning percutaneous translumbar aortography, Lindgren (1953) has pointed out that even if a trial injection of a small quantity of contrast medium shows it all in the lumen of the vessel, some may nevertheless be injected paravascularly during the main injection. Several factors may be involved. If the injection is made with great force, purely mechanical displacement of the needle in relation to the aortic wall may occur, or the rapid injection of a very hypertonic solution may stimulate and cause contraction of the vessel, with the result that the needle tip, if close to the wall, may be displaced into its substance. Aortic pulsation and uncontrolled respiratory movement are further possible causes for displacement of the needle-tip during aortography.

Although a trial injection of a small quantity of contrast medium appears to be an additional safeguard, it should not be forgotten that there is an inevitable delay of three to five minutes for the development of the radiograph. During this time respirations must be resumed and displacement of the needle-tip may occur.

Another device which has been used to avoid intramural injection is a needle with a sealed end and two lateral openings. It is conceivable, however, that when such a needle is inserted obliquely into the aorta, while one orifice may be well in the lumen of the aorta and allow free reflux of blood, the other may lie within the wall so that subsequent injection may cause some dissection, though it is likely to be less than with an orthodox needle.

Conclusion

Fatal complications following percutaneous lumbar aortography are still being reported, in spite of refinements of technique and the exercise of great care. From our experiments it seems likely that aortic dissection could account for a number of these fatal complications. From examination of published radiographs we are convinced that minor degrees of aortic dissection are quite common, although not commented on by the authors, perhaps because the significance is not appreciated.

Summary

A complication of aortography—aortic dissection—is described in which a part or the whole of the contrast medium is injected into the media of the aorta.

Experimental evidence is produced which explains the mechanism of this aortic dissection and demonstrates that this complication is analogous to a spontaneous dissecting aortic aneurysm.

This complication is important for three reasons. It may give rise to misinterpretation if its true significance is not appreciated, since it may closely simulate arterial thrombosis. There may be serious sequelae. It may occur in spite of the most scrupulous technique.

REFERENCES

- Antoni, N., and Lindgren, E. (1949). *Acta chir. scand.*, **98**, 230.
 Boyarsky, S. (1954). *J. Amer. med. Ass.*, **156**, 599.
 Fariñas, P. L. (1941). *Amer. J. Roentgenol.*, **46**, 641.
 Lindgren, E. (1953). *Acta radiol. (Stockh.)*, **39**, 205.
 Maluf, N. S. R., and McCoy, C. B. (1955). *Amer. J. Roentgenol.*, **73**, 533.
 Melrose, D. G. (1953). *British Medical Journal*, **2**, 57.
 Miller, G. M., Wylie, E. J., and Hinman, F. (1954). *Surgery*, **35**, 885.
 Peirce, E. C. (1951). *Surg. Gynec. Obstet.*, **93**, 56.
 Robinson, A. S. (1956). *A.M.A. Arch. Surg.*, **72**, 290.
 dos Santos, J. C. (1955). *L'Angiographie rénale*. Angiografia Renal. Atenas.
 dos Santos, R., Lamas, A. C., and Pereira Caldas, J. (1929). *Med. contempor.*, **47**, 93.
 Seldinger, S. I. (1953). *Acta radiol. (Stockh.)*, **39**, 368.
 Smith, P. G., Rush, T. W., and Evans, A. T. (1951). *J. Urol.*, **65**, 911.
 Wagner, F. B., jun., and Price, A. H. (1950). *Surgery*, **27**, 621.
 Weisman, A. D., and Adams, R. D. (1944). *Brain*, **67**, 69.

COMPARISON OF TETRACYCLINE WITH CHLORTETRACYCLINE IN TREATMENT OF PNEUMONIA REPORT FROM THE CITY GENERAL HOSPITAL, SHEFFIELD*

The effectiveness of chlortetracycline ("aureomycin") is well established in the treatment of pneumonia. The Medical Research Council report (1951) indicated, however, that a proportion of patients treated with the antibiotic develop unpleasant side-effects, particularly affecting the gastro-intestinal tract. Further experience showed that satisfactory blood levels could be obtained with a dosage lower than that used in the original trials, and Finland, Grigsby, and Haight (1954) found that the incidence of toxic effects was thereby reduced, although not eliminated.

Reports from America by Finland, Purcell, *et al.* (1954) and Wood *et al.* (1954) suggested that tetracycline, closely related in its chemical structure to chlortetracycline and oxytetracycline ("terramycin"), might have certain advantages over them in that it was claimed to possess greater chemical stability and lower toxicity in a dosage producing effective blood levels. This has been confirmed by McCorry and Weaver (1955) in this country.

An opportunity arose to study the behaviour of two of the tetracycline group of drugs, tetracycline and chlortetracycline, in cases of clinical pneumonia, and the purpose of this paper is to record the response obtained in a controlled trial, with special reference to drug toxicity.

Methods

The procedure followed that outlined in the M.R.C. report (1951), in which this hospital also participated.

Type of Case.—All patients admitted with clinical pneumonia to the adult medical wards of the City General Hospital, Sheffield, were included in the series, with the exception of (1) those aged 70 years or more, (2) those already convalescent, (3) those in whom the pneumonia was associated with heart failure, and (4) those who had received treatment with an antibiotic or a sulphonamide for longer than the 24 hours preceding admission. To confirm the diagnosis a chest radiograph was taken as soon as possible after admission. In a number of cases this showed the initial clinical diagnosis to be incorrect, and these cases

*Those taking part in the study were:—*Clinicians*: Drs. C. S. Darke, F. J. Flint, R. W. Meikle, and J. E. Middleton; *Bacteriologists*: Drs. E. H. Gillespie, M. Pownall, and J. E. M. Whitehead; *Haematologist*: Dr. S. Varadi; *Pathologists*: Drs. G. D. Powell and A. J. N. Warrack; *Radiologists*: Drs. E. K. Abbott and A. B. Black.