a primary gene mutation having occurred in one of the patient's paternal grandparents. Such families are the rare exception to the rule that one case discovered invariably reveals a score more.

SUMMARY

Two cases of hereditary onycho-osteodysplasia are presented. The rare association of exostosis with the syndrome is described. The statement that joint dysplasias occur only in association with nail lesions is shown to be only partly correct. Genetic hypotheses are discussed in relation to the possibility of recent primary gene mutation.

I wish to express appreciation to Prof. Josse Kaye for permission to publish, and to Dr. J. N. Jacobson for final correction of the draft, also to Dr. C. A. Noble who provided the clinical details, and the Photographic Unit for its reproduction of the X-rays. I should like to thank Miss N. Warren and Miss A. Davies for their unstinting help in regard to the radiography and secretarial assistance.

REFERENCES


NEW RADIOLOGICAL CONTRAST MATERIALS AVAILABLE IN SOUTH AFRICA

—A PRELIMINARY COMMUNICATION


A new range of radiological contrast materials has become available recently for general use in South Africa. Being manufactured locally under licence from the parent factory in Italy (Bracco), it offers a safe and extremely good contrast material which will be economical in use. Three basic types of contrast material are currently in use for intravenous pyelography and angiography. The two newer agents, iothalamate and metrizoate, have been added to the more widely used diatrizoate compounds. Chemically, the agents in common use at present fall into the following three groups:

(i) Diatrizoate

(e.g., Hypaque and Urographin. 62% I.

(ii) Iothalamate

(e.g., Conray. 62% I.

(iii) Metrizoate

(e.g., Triosil. 60.5% I.

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Metrizoate and iothalamate are chemically similar to the widely used diatrizoate and differ only in one of their side-chains. Diatrizoate and iothalamate have an identical iodine content (62%) and metrizoate has a slightly lower content (60.5%). In a recent communication, Fischer and Cornell' found that the methylglucamine salts of the above compounds were better tolerated than the sodium compounds. An example of the former is Cardiographin 85% and the latter is marketed as Hypaque 50. Mixtures of sodium and methylglucamine diatrizoate are found in Urografin and Hypaque 90. Conray 280 is methylglucamine iothalamate and Conray 420 and 480 comprises sodium iothalamate. Sodium metrizoate goes by the trade name of Triosil. Because of their lower toxicity, which was found by measuring the changes in heart rate and arterial blood pressure after intracarotid arterial injection, the methylglucamine compounds are recommended for carotid angiography in preference to the sodium-containing iodides. Of all the sodium-containing agents they also found that sodium diatrizoate was the best tolerated.

Recently we were offered a limited quantity of a new range of contrast material for clinical trial and evaluation. This paper therefore serves as a preliminary communication to report on our findings with these materials.

INTRAVENOUS PYELOGRAPHY

This substance which is also a tri-iodide differs from the above three compounds in general use and goes by the generic name of iodamide. It is a 3-acetoaminomethyl-5-acetylamino-2,4,6-triiodo-benzoic acid and has the following structural formula:

$\text{C}_6\text{H}_5\text{C}(-\text{CH}_2\text{CO})_3\text{NHCF}_3\text{I}_3$
It is marketed under the name of Neo-Uromiro and two forms are currently available: Neo-Uromiro 300 and Neo-Uromiro 380. The former has 49.5 G/ml. iodamide and 64.9 G/ml. N-methylglucamine salt of iodamide, with an iodine content of 300 mg./ml. Neo-Uromiro 380 comprises 62.79 G/ml. iodamide, 69.96 G/ml. N-methylglucamine salt and 10.02 G/ml. sodium salt of iodamide with an iodine content of 380 mg./ml. (Fig. 1). It can therefore be seen that there is a considerable difference in the chemical structure of the iodamide compounds when compared with the more widely used contrast materials.

Numerous studies have appeared in the Continental literature on the toxicity and clinical effectiveness of iodamide, but to our knowledge this is the first report to appear in the English language. Iodamide has been widely studied both with experimental animals and in clinical trials. Bonati et al. concluded that by intravenous and intraperitoneal administration in mice, rats, guinea pigs and rabbits, its toxicity is of the same order and often lower than iothalamate and diatrizoate salts. The alterations in the ECG and the arterial blood pressure after the intravenous injections of sub-toxic doses of iodamide (10 - 15 ml./kg. of 50% solution) were very transient. It was also very well tolerated when administered intracerebrally. The hypotensive activity and peripheral vasodilation were less than that found with the more usually employed urographic contrast media and it was also seen that renal excretion was very high, especially during the first few minutes. Würdinger concluded in clinical trials that these preparations may be considered an ‘excellent contrast medium for intravenous urography due to the minimum toxicity, rapid renal excretion, low viscosity and good contrast’. Best visualization of the urinary tract was obtained on the radiographs from 3 to 10 minutes after the end of the injection. It is noteworthy at this stage to point out that both Würdinger and Grothuesmann quite definitely relate the onset of side-effects to the injection period of the intravenous injection.

They have both found that when the contrast material is injected rapidly (20 - 30 seconds) without prior sensitivity tests, the reactions to contrast materials are definitely reduced as compared with long injection times, as they claim that the excitation threshold is exceeded and there is insufficient time for antibody formation. Rapid injection times have also been used by Glanville and Herlinger who inject 50 ml. iothalamate within 45 secs.

For the purpose of this study, intravenous pyelograms were performed after withholding food and fluids for at

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**Fig. 1.** Stricture of the right pelvo-ureteric junction (Neo-Uromiro 300).

**Fig. 2.** Normal IVP. Note the good display of entire renal collecting system (Neo-Uromiro 380).
least 6 hours and a bowel wash-out was used for all cases to eliminate colonic faeces (Fig. 2). Tomography, zonography and ureteric compression were utilized where indicated. Iodamide was used in 20 ml. doses and the results were analysed by at least two observers in consultation. If a dispute arose, the more conservative opinion was used for this study. Neo-Uromiro 300 was used for IVP in 170 cases. Contrast visualization was adjudged as excellent in 99 cases, good in 61 cases, adequate in 5 cases and poor in 5 cases. Of the 5 cases which gave poor visualization, 2 had stag-horn calculi, 1 had a blood urea of 196 and 2 patients were very obese. As a result of the intravenous injection of 20 ml., there was no reaction in 158 cases, 11 patients complained of mild nausea and 1 patient vomited. There were no serious reactions and no supportive therapy was required for any of the 170 cases. Purposeful injection of 2 ml. of iodamide into the soft tissues produced no untoward reaction or complaint from two patients.

Neo-Uromiro 380 was used in 28 cases for IVP. Visualization was excellent in 16, good in 8, adequate in 2 and poor in 2 cases. The only reactions to the contrast were slight nausea in two patients. Neo-Uromiro 380 produces a high degree of excellent visualization of the renal collecting tracts, but is rather viscous. Comparative tests give the following readings:

<table>
<thead>
<tr>
<th>Medium</th>
<th>CPS at 37°C (counts/sec.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypaque</td>
<td>50 230</td>
</tr>
<tr>
<td>Conray</td>
<td>60 394</td>
</tr>
<tr>
<td>Urografin</td>
<td>60 406</td>
</tr>
<tr>
<td>Neo-Uromiro300</td>
<td>58</td>
</tr>
<tr>
<td>Angio-Conray</td>
<td>798</td>
</tr>
<tr>
<td>Urografin</td>
<td>76 889</td>
</tr>
<tr>
<td>Neo-Uromiro380</td>
<td>107</td>
</tr>
<tr>
<td>Hypaque</td>
<td>90 1920</td>
</tr>
</tbody>
</table>

Krovetz et al., in a study of factors determining the delivery rates in cardiac catheters using various contrast media, found that the delivery rate was inversely proportional to the square root of the length of the catheter and it increased non-linearly with the pressure of the injection and radius of the catheter. Viscosity per se was found to be less important than the inverse relationships predicted by the laminar flow theory. Although superficially Neo-Uromiro 380 appears to be more viscous than most triiodides, in practice it is found that viscosity is purely a function of temperature and that if the solution is adequately warmed before injection the viscosity is diminished dramatically.

CHOLECYSTOGRAPHY

Cystobil is the name of the preparation available for the oral route. This medium is in the form of tablets of 0.5 G each and the usual adult dose is 3 G. Chemically, Cystobil is α-ethyl-β-(3-amino-2,4,6-triiodophenyl)-propionic acid and bears the following structural formula:

As can be seen, this bears a close relationship to the more commonly used iopanoic acid (Telepaque) which comprises 3-amino-α-ethyl-2,4,6-triiodohyrocinnamic acid (USP) with the structural formula thus:

![Structural formula of 3-amino-α-ethyl-2,4,6-triiodohyrocinnamic acid](image)

Cystobil is used in the manner and dosage of iopanoic acid with radiographs being exposed usually 15 hours after taking 3 G by mouth. A total of 56 cases were examined using Cystobil. Forty-two cases produced good visualization of the gallbladder and this included the routine use of fluoroscopy in the erect position with spot films also in the lateral posture. Poor visualization occurred in 9 cases, which required double-dose examinations (6 G taken on two consecutive evenings), and no contrast was seen in the gallbladder in 5 cases. No serious reactions were encountered and no serious vomiting or diarrhoea was reported by the patients. It was noted on the films that the contrast was generally very good and that colonic residual contrast was very low (Fig. 3).

Endocystobil Forte is a 50% solution of methylglucamine iodipamide in a water-soluble base for intravenous injection and is offered for use in intravenous cholecystography. This material was used in 19 cases with excellent visualization of the bile ducts in 12 cases, adequate visualization in 2 cases and poor contrast in 5 cases. No serious reactions occurred in any of the 19 cases and only two patients complained of slight nausea after the injection which soon disappeared without any supportive treatment.

HYSTEROGRAPHY

Twelve hysterosalpingogram examinations were performed with the use of iodamide. They all produced excellent contrast on the films. Only one patient had symptoms and she complained of severe abdominal pain due to peritoneal...
spill. The other patients were symptom-free during the examination.

MISCELLANEOUS

Iodamide was used for 2 'T-tube' postoperative cholangiograms producing excellent results. Two retrograde voiding cysto-urethrographies also produced satisfying results. Only two arteriograms were performed with iodamide; the first of which was a renal arteriogram and the second was a femoral arteriogram with a Seldinger catheter at the abdominal aortic bifurcation. The contrast and visualization in both was excellent, but the latter patient developed nausea and a transient drop in the arterial blood pressure after the first injection.

DISCUSSION

As can be deduced from the aforegoing, this is a preliminary communication after a short clinical trial with only a limited quantity of contrast material for radiological use which has been recently announced in South Africa.

Our results have confirmed the reports in the literature pertaining to the excellence of these products and their low toxicity. We have found a very high degree of tolerance, very few systemic side-reactions and very little local reaction when injected into the tissues. Iodamide is a new development and the two solutions offered are excellent for intravenous urography and arteriography. Its low toxicity would suggest particularly its safety for cerebral arteriography.

In intravenous pyelography, we have been particularly impressed by the density produced on the radiographs which has been much more pleasing and informative than when the other urographic agents have been used. The rapid renal excretion is particularly valuable when examining young children and ill patients.

From reports in the literature, it would appear to be an excellent solution for cardiac angiography. Angio-Conray which, perhaps, offers the most ideal iodine content (480 mg./ml.) coupled with its low viscosity has unfortunately resulted in severe reactions, and several cases of ventricular fibrillation have been reported. This has resulted in the parent firm Mallinckrodt marketing a product with a lower iodine content (400 mg./ml.) either as a pure sodium salt or sodium methylglucamine mixture. However, these products are not intended for cerebral angiography.

Although the results of the cholegraphic agents are not statistically valid, the few cases we have studied attest to their potential and confirm previous reports as to their clinical value.

Iodamide was also used in several other contrast examinations and has been found to produce excellent contrast and visualization with a low incidence of reactions.

SUMMARY

A preliminary report of new contrast materials now available in South Africa has been made. The principle agent, iodamide, is available either as a methylglucamine, iodamide mixture (Neo-Uromiro 300), or methylglucamine, sodium iodamide mixture (Neo-Uromiro 380).

A series of 198 intravenous urographies using these compounds show that good visualization of the renal collecting tracts occurred in 93% of cases and adequate contrast occurred in 3.5%, therefore producing diagnostic results in 96.5% of cases.

Fig. 4. Same as Fig. 3 with the renal outlines pencilled in to show more clearly the renal outline which was very clearly seen on the original radiograph.

Fig. 5. Intravenous cholecystangiogram. The arrows point to three non-opaque calculi in the common bile duct. Note the good filling of the gallbladder 35 minutes after the injection of 20 ml. of Endocystobil Forte.

Iodamide was also used for arteriography, hysterography, postoperative 'T-tube' cholangiography and retrograde cysto-urethrography with satisfactory results.
The use of Cystobil for oral cholecystography and Endocystobil Forte for the intravenous route produced excellent results in the limited number of cases examined.

We should like to express our thanks to Satab Laboratories (Pty) Ltd. for the supply of the above contrast agents, and their help with the translations of the articles which we have quoted. We also acknowledge the help of our colleagues, Drs. E. Alan Price, Harold J. Bloch and John Gold for their unswerving help with the evaluation of the results and their encouragement.

Gynaecography

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'Gynaecography' is the term used for radiographic demonstration of the ovaries, fallopian tubes, uterus and uterine-supporting ligaments. Some authors have included simultaneous opaque-medium hysterosalpingography in the term, but today gynaecography is accepted as meaning gas-contrast pelvic organ examination.

Lorey1 described the use of intraperitoneal air to demonstrate abdominal organs radiologically in 1912, and in 1920 Alvarez2 introduced the use of the safe gas carbon dioxide for this purpose and described how the patient could be positioned to demonstrate the pelvic organs. Von Zwaluwenberg and Peterson3 used gynaecography extensively and reported a large series in 1921, while 1,000 cases were reported by Stein in 1932. In 1935 Stein and Leventhal4 published the details of a group of cases of the syndrome of amenorrhoea, sterility and hirsutism which now bears their name.

Gynaecography is widely used in the USA but there are few British references to the subject5 and in South Africa the examination was virtually unknown until we began investigating patient's early in 1964 after having had experience with the method in Boston. The increasing popularity of gynaecography among Johannesburg's gynaecologists is due in no small measure to the interest of Dr. Joel Cohen, who, although initially sceptical, has become a most enthusiastic advocate of the examination and with whom we are presently engaged in a correlative study. Our experience so far includes more than 150 examinations.

Indications

Gynaecography is indicated in female patients of any age in whom accurate assessment of the size of the uterus and ovaries is required and particularly when accurate bimanual examination is impossible such as in infants and children, in virginal and obese women, in patients with a narrow introitus or patients who are so tense that examination is unsatisfactory. There are 3 main groups of indications:

1. Hormonal disorders and infertilty: Stein-Leventhal syndrome (Fig. 3), virilism, adrenogenital syndrome, sexual precocity6, primary amenorrhoea, gonadal dysgenesis, hypogonadism (Fig. 4), delayed puberty, hypopituitaryism and pituitary dwarfism and reassessment of ovarian size after wedge resection.

2. Developmental anomalies of the genital tract: urogenital sinus development anomalies—stenosis and atresia of the vagina, congenital absence of the uterus, demonstration of gonads and uterus in pseudo-hermaphroditism and differentiation of separate from bicornuate uterus.

3. Investigation of pelvic masses: uterine fibromyomata and carcinoma, ovarian tumours and cysts (Fig. 5), broad ligament masses, unruptured ectopic pregnancy, fallopian tube masses, staging of cervical carcinoma7 and endometriosis.

Contraindications

Acute intraperitoneal haemorrhage, acute pelvic sepsis, cardiac or respiratory disease of such severity that the pneumoperitoneum or steep head-downward tilt of the patient cannot be tolerated.

Technique of Performing Gynaecography

Apparatus

An X-ray table with myelography shoulder rests and leg strap is used which can be tilted to at least 45° from the horizontal, with undercouch Potter Bucky grid and overcouch tiltable X-ray tube. One requires a cylinder of nitrous oxide with suitable reducing valve and gas-flow tap, sterile connecting rubber or vinyl tubing, a three-way stop-cock with attached 50 ml glass syringe and a flexible connector from the stop-cock to the puncture needle which may be a 19-gauge short bevel spinal needle, or our preference, a Sheldon8 carotid puncture trocar and cannula. Sterile draping towels, antisepsic skin paint, a syringe and suitable needles for local anaesthesia are required and a sharp-pointed scalpel blade. We use a 100 cm. rule to measure the focus-film distance and a 45° spirit-level to check the inclination of the X-ray couch.

Preparation

The patient is admitted in a fasting state to the ward an hour or two before the procedure, which is explained to her in order to allay her anxiety. The bowel is cleansed by the use of one or two Dulcolax tablets given the night before the examination, and on admission a soap and water enema is given to clear the sigmoid colon and rectum. We cannot stress sufficiently the importance of adequate bowel preparation to ensure the success of the examination. The patient empties her bladder immediately before being placed on the X-ray table.

Premedication

Phlegmatic patients require no premedication but we give nervous women 1½ gr. of Secional orally an hour