inhalation anaesthetics. He considers evipan far superior to anything he has previously experienced.

In the stress of circumstances it is possible for a surgeon to give the anaesthetic and carry on the operation with a minimum of nursing assistance and practically no danger to the patient. Evipan may be given without danger with a partially full stomach. Owing to the great rapidity of induction, the total time required for an operation is very materially reduced, especially with several consecutive short operations.

Special Advantages in Ophthalmic Surgery

The whole of the face and head is left free for the surgeon, which is a considerable help in eye operations. As most ophthalmic operations are of short duration, a single evipan injection is peculiarly suitable to most such. We have found it very suitable for cases of squint in children, for excisions and eviscerations of the eyeball, for acute glaucoma, plastic operations—in short, for practically all eye operations *where a general anaesthetic is advisable*.

Under evipan anaesthesia the intraocular tension falls, both in eyes with normal tension and in those with raised tension. This was demonstrated in selected cases in our series by palpation and by the use of the Schiotz tonometer. This is a very advantageous factor in operations for acute glaucomatous conditions. In a considerable number of ophthalmic operations the subjects are old, enfeebled persons, perhaps suffering from diabetes, tuberculosis, or other constitutional diseases, in whom inhalation anaesthesia frequently involves grave risks. In the majority of these cases evipan may be given with safety, with every satisfaction to the patient and surgeon alike.

Analysis of Our Series, with Comments

1. *Excision of Eyeball*.—Evipan is ideal for this operation, and we have now adopted it as the routine method of anaesthesia. Thirty-nine operations were done, the age of the patients varying from 30 to 85 years. Particular mention should be made of the advantages over inhalation or local anaesthesia in the following cases:

(a) I. B., male, aged 58 years, an advanced case of Graves' disease with chronic iridocyclitis from corneal ulceration, due to severe proptosis.

(b) A. S., male, aged 66 years, severe arteriosclerotic and hypertic, with recent hemiplegia and mental changes.

(c) W. J., male, aged 72 years, very feeble patient with myocardial degeneration and chronic bronchitis.

In all these cases anaesthesia was most satisfactory, and there were no untoward after-effects. Another patient, M. P., male, aged 65 years, was feeble and cachectic, and clinically his liver contained large masses of secondary growth. He was given evipan for removal of a secondary glaucomatous and painful eye, the seat of a primary malignant melanotic tumour. No ill effect followed, although it is said that severe liver disease is a contraindication to the use of evipan.

2. *Evisceration of Eyeball*.—Nine cases, age of patients varying from 9 to 75 years.

3. *Operations for Glaucoma*.—Six cases, consisting of four trephines, one Lagrange's operation, and one posterior sclerotomy. The only difficulty here, as in any general anaesthetic, is the tendency of the eyeball to roll upwards, although this tendency is much less noticeable with evipan than with inhalation anaesthesia. We have found that the intraocular tension is always lowered; this is easily demonstrable by palpation, and we have shown it conclusively by the Schiotz tonometer to be reduced by as much as 10 mm. in some cases.

4. *Lid Operations and Plastic Operations on Sockets*.—Eight cases. The great advantage here is that distortion of the eyelids with local injection fluid is avoided. One case, J. W., male, aged 66 years, underwent a successful operation for paralytic ectropion (due to facial palsy complicating middle-ear disease), fascia lata strips being taken from the thigh and used as slings. The operation lasted one and a quarter hours, and anaesthesia was satisfactory throughout, the total

amount injected being 14.5 c.cm. (given in two successive injections). Another case worthy of mention was H. S., male, aged 43 years, suffering from fibroid phthisis, who underwent a "plastic operation on socket" with good result.

5. *Squint*.—Twenty cases, consisting of eighteen "tenotomies and advancements" and two tenotomies. In one case, a nervous female aged 18 years, operation was commenced under local anaesthesia, but the patient was unable to keep still, and so an injection of evipan was given immediately, and the operation proceeded with satisfactorily. Inhalation anaesthesia would have been impossible owing to the fact that the patient had recently had a meal. Evipan has not been used very considerably for squint, because for obvious reasons local anaesthesia is to be preferred when the patient is sufficiently old to exercise self-control.

6. *Attempt to Remove Deep Intraocular Foreign Body*.—One case; satisfactory anaesthesia.

7. *Opening of Lachrymal Abscess*.—Three cases.

Summary

1. The advantages of intravenous anaesthesia with evipan in ophthalmic surgery are shown.

2. A series of eighty-six cases is presented, showing very satisfactory results with no complications.

We are indebted to the members of the honorary staff of the Royal Westminster Ophthalmic Hospital for their kind co-operation in the use of evipan for their cases.

CHORIONIC CARCINOMA

WITH A REPORT OF A CASE FOLLOWING RUPTURED TUBAL GESTATION

BY

RUFUS C. THOMAS, F.R.C.S.ED., M.C.O.G.

Cases of chorionic carcinoma are always of sufficient interest and rarity to merit publication. According to DeLee¹ "hydatidiform mole preceded the development of this disease in 33 to 40 per cent. of reported cases." Again, Eden and Lockyer² state that "in two out of every three cases the immediately preceding pregnancy terminated in abortion." Both the above statements presumably refer to uterine pregnancies. The urgent symptom would therefore be uterine haemorrhage, and the fact that it was preceded by an abortion, either of the ordinary type or more especially of a hydatid mole, would tend to put one on guard. Chorion, wherever situated, may, however, be liable to malignant degeneration. DeLee¹ states that "ectopic gestation may undergo this [hydatidiform] degeneration." Tubal and ovarian pregnancies must therefore share in the general danger.

Chorionic Carcinoma of Tube or Ovary

The clinical picture of a malignant degeneration of a chorion situated in the ovary or tube is nevertheless very different from that of the uterine variety. Such cases must be very rare indeed, and, occurring as they do without the usual symptoms of the uterine type, coupled with the fact that the growth is hidden away in the abdominal cavity, must give rise to much confusion in diagnosis. There is not always uterine bleeding to warn the patient that something is wrong. Advice would tend to be sought late, thus giving further time for the condition to develop. Pain in the abdomen or the presence of a tumour in the lower abdomen following an operation for ectopic pregnancy would be the probable reason for seeking advice.

The literature yields the following information. Risel³ collected eleven cases of primary chorio-epithelioma of the tube, and reports a case of chorio-epithelioma developing in the pelvis, proved at subsequent operation two

and a half months after removal of tubal gestation (about six and a half months after this had started). The woman died shortly after the second operation, and a post-mortem examination showed no growth in uterus or genitalia, but metastases in liver and lungs. Liepmann⁴ reported seven more. In one case recorded by Davidsohn⁵ chorio-epithelioma formed in the stump of a tube excised for ruptured tubal gestation. Lefquist⁶ gives an account of a tubal pregnancy removed from a tube which was left *in situ*. Two years later a pregnancy recurred in the same tube, which was removed. Pathological examination revealed an early primary chorio-epithelioma of the tube. Hartz⁷ described a case of ruptured tubal gestation in which there were extension of chorionic epithelium into the wall of the tube and chorionic epithelial cells in the lumina of some of the veins. The patient was well two years afterwards. In his paper Hartz states that "primary chorio-epithelioma of the Fallopian tube is of comparatively frequent occurrence when we take into consideration that tubal gestation forms but a small proportion of all uterine pregnancies. Of 300 chorio-epitheliomas up to 1905 the primary tubal variety comprised 3.5 per cent." He also states that "metastatic growths occur from tubal growths just as readily as they do from the uterine variety."

Vaginal Metastasis

Duggan,⁸ in the report of his case, says that the patient came for treatment of "a rather friable, purplish swelling on the right vaginal wall. A mass was felt in the left vault, not movable, irregular, and slightly tender. Uterus slightly enlarged." Removal of both ovaries and tubes and supravaginal hysterectomy were carried out. The left tube was ruptured. Pathological examination showed chorionic carcinoma. X-ray and radium treatment were given, and when the patient was seen two years later "pelvic examination revealed no sign of recurrence—she had gained weight and strength." Bethel Solomons and Smith⁹ recorded a case almost identical with Duggan's, and both are very interesting in that a vaginal metastasis was present at the time advice was first sought. Solomons and Smith seem to have been in doubt as to whether their case was secondary to tubal gestation, as "the chance of it being secondary to tubal pregnancy is most doubtful, for her periods had always been absolutely regular." But the history they give surely does not agree with this, for they state "she was sent to hospital because of continuous haemorrhage since her last menstruation, which had started three weeks before admission." Obviously her last period was most irregular. And, equally obvious, before admission she could have had a tubal pregnancy of nearly six weeks' duration which ruptured three weeks before the patient was seen by them. Chorionic carcinoma may have developed at any time within these limits. It is even possible that the previous (?) normal menstrual period was really uterine bleeding associated with a small unnoticed attack of pain due to commencing rupture of the tube.

Miles Phillips¹⁰ had a case of ruptured left tube, with "a small nodule of adherent blood clot on the bladder wall." Tube and nodule were excised. After chorionic carcinoma had been demonstrated microscopically the uterus was curetted, nothing abnormal being found. Six weeks later there was recurrence in the left broad ligament, "an ovoid purplish nodule in the anterior vaginal wall," and a nodule on the bladder wall at the site of the previous nodule. There was also a mass at the root of the mesentery of the small intestine. Total hysterectomy with removal of broad ligament growth, all appendages,

and the bladder nodule was then done. The mesenteric growth was irremovable. All these showed chorionic carcinoma. Three years later she was alive with no signs of recurrence in the abdomen or elsewhere. Fleurent,¹¹ in his case report, quotes Risel's twelve cases, and says that accounts of twenty others were given between 1905 and 1930. If we add his case, Duggan's, Stein's, and mine, the number up to date would appear to be at least thirty-six.

Pathology

It is interesting to recall that Marchand divided the disease into two groups—atypical or benign, and typical or malignant. The benign is characterized by comparative or complete absence of Langhans's cells, and to this type Ewing gives the name "syncytioma." Lynch and Maxwell¹² state "the prognosis in syncytioma is essentially favourable, since the process advances slowly, and the life of the wandering cells is short." Referring to the malignant type, they say "the tumour seems to have a more rapid course, and to metastasize more quickly than does chorio-epithelioma of the uterus. Albert's case and that of Hartz are the only ones which recovered." Duggan's and Phillips's cases are apparently two more.

The degree of malignancy seems to depend on the presence of proliferating and atypical cells of Langhans's layer, which are always present in the malignant type, even in the metastases. Secondaries may be found in the abdomen, spleen, lungs (very common), liver, vertebral column, vagina, and brain. Ovarian changes associated with the disease are well known. Lynch and Maxwell¹² say "there is no doubt but that pronounced cystic changes in both ovaries occur so frequently with chorio-epithelioma as to constitute a specific anatomical feature of the disease." In this connexion, Friedlander¹³ quotes Zondek and Aschheim, and Evans and Smith, as showing this formation of lutein material to take place after implantation of anterior pituitary and ovarian substance in animals, and Murati and Adachi as having produced the same results with the placenta. Urine from a case of chorionic carcinoma may contain as much as 500,000 mice units of anterior pituitary hormone per litre, compared with 8,000 to 12,000 units in normal pregnant urine. Does this excess of hormone hold the secret of both chorionic carcinoma and lutein cyst formation?

Friedlander also quotes Oskar Fraenkl as showing that the serum of a normal pregnant woman is able to destroy foetal tissue from placenta, liver, or kidney, while the serum of a woman suffering from chorio-epithelioma does not possess this lytic action. He concluded that the formation of chorio-epithelioma is due to the absence from the blood of the pregnant woman of the syncytiolytic properties of the serum, and believes that spontaneous cures are due to a recovery of these properties. We do not know what limits the normal invasive power of the chorionic epithelium. That there must be some limiting agent is obvious. If Fraenkl's theory holds the explanation, it could be proved by the injection of serum from a normal healthy pregnant woman into a series of cases of chorionic carcinoma. Such a serum would be very easily secured. Theoretically, it should be obtained from women three to four months pregnant, when limitation of the invasive power of the chorionic epithelium should be taking place and the syncytiolytic properties of the serum presumably be at their height. As a control, estimation of the urine as regards the number of mice units (Aschheim-Zondek) of anterior pituitary hormone might be made, and only that serum the urine of whose donor contained less than 12,000 units be used for the purposes of treatment.

History of Case

The following is the history of my case of ruptured tubal pregnancy which was followed by chorionic carcinoma.

The patient, a Hindu, was admitted into the Irwin Hospital, Jamnagar, suffering from pain in the abdomen, with slight, dark-coloured haemorrhage from the uterus. She had missed two periods. Examination revealed a small tender mass in the region of the right tube, and a diagnosis of ruptured ectopic gestation was made. I operated upon her the same day, and found a tubal gestation which had ruptured intraperitoneally. There was not a great quantity of free blood, and not many clots. The tube was removed, the clots were cleared out, and the abdomen was sponged dry and then closed. Her immediate convalescence was uneventful, and she left the hospital three weeks later.

Two months afterwards she was again admitted. She was now looking very ill, and complained of a swelling in the right side, with considerable pain in the lower abdomen. There was no haemorrhage or discharge from the uterus. Palpation confirmed the presence of the tumour in the right pelvic region, and vaginal examination showed that the tumour was in very close proximity to the uterus, which was enlarged to the size of a three-months pregnancy. The upper surface of the tumour reached well above the brim of the pelvis. The woman had lost weight appreciably, and was looking anaemic and obviously worried. I opened the abdomen again, and found the whole of the right side of the uterus and the right broad ligament covered with a soft, friable, dark-grey-coloured growth. Its nature was only too obvious. It had already begun to spread towards the bladder, and there were several small masses on the peritoneum of Douglas's pouch. The right cornu of the uterus was the seat of a somewhat larger mass, and a small piece was taken from this situation for microscopical examination. There was no possibility of benefit from excision of the uterus, as this would have only taken away about a quarter of the growth. The bladder and Douglas's pouch were already involved. The site of the ectopic was a mass of growth. The abdomen was closed on the tragic sequel to what had been a successful operation for ruptured ectopic gestation. The small piece which had been removed was sent to the Haffkine Institute, Bombay, and a report was received ten days later, confirming that the growth was chorionic carcinoma. The slide which the director of the institute sent me was typical of chorionic carcinoma of the uterus.

At this time it struck me that a few doses of deep x rays might do the patient some good. They could, at any rate, do no harm, and there was no other possible method of treatment. She was therefore sent to the x -ray department, where she received two "massive" doses at intervals of three weeks. I left India about a fortnight after the second dose, so am unfortunately not able to give any later information than up to this date. At this time, however, the tumour had definitely begun to retrogress, and was about half the size it was on admission. The patient's general condition was also much better, and her pain was decidedly less. Locally, therefore, deep x -ray therapy had certainly had some beneficial effect. There was always the possibility of metastasis having already taken place, but clinically there had been no signs of this. I do not know whether deep x -ray therapy was continued after I left Jamnagar. In view of the benefit already experienced it is to be hoped it was.

Summary and Discussion

Though the story must remain unfinished the following conclusions can be drawn:

1. Ruptured tubal pregnancy, removed by operation, was followed within a very short time by malignant disease of the chorion.

2. Three months after operation the growth had become palpable above the pelvic brim, and was found at the second operation to have involved the whole of the right broad ligament, the right pole of the uterus, the bladder, and Douglas's pouch.

3. The symptoms were: lower abdominal pain, cachexia, and a tumour in the right iliac fossa. There was no uterine bleeding or discharge.

4. Two "massive" doses of deep x -ray therapy resulted in definite retrogression of the tumour, considerable lessening of pain, and improvement in the general condition of the patient.

To my mind there are three possible ways in which this case can be explained. In considering them we must remember that we are dealing with a gestation sac which had ruptured into the peritoneal cavity. The possibilities are as follows:

1. During the rupture chorionic elements may have been "sprayed" over the surrounding parts, especially the right broad ligament and the pouch of Douglas. These underwent malignant degeneration later.

2. Chorionic carcinoma may have begun to develop before the actual rupture took place, with the result that malignant cells were directly spread over the broad ligament and Douglas's pouch.

3. This type of growth extends via the veins. Although scattering of malignant cells may not have taken place, the veins of the broad ligament may nevertheless have been packed with syncytial and Langhans's cells spreading in all directions. These would have gone on proliferating after removal of the ruptured ectopic gestation. An earlier stage of this condition would appear to have been present in Hartz's case.

Lastly, the interesting question arises as to the "receptive," or perhaps I should say "resistive," qualities of the pelvic peritoneum in a condition of this sort. We know that the pelvic peritoneum is far more resistant to infection than that of the upper abdomen. But the pelvic peritoneum during the period of pregnancy is not in quite the same condition as it is in the non-pregnant state. There is a much increased blood supply, and all the pelvic organs are in a much more "luscious" condition. May it not, therefore, on this account provide a more "receptive" nidus for the malignant cells showered over it?

REFERENCES

- ¹ DeLee, J. B.: *Principles and Practice of Obstetrics*, 1933.
- ² Eden and Lockyer: *Gynaecology for Students and Practitioners*.
- ³ Risel: *Zeit. f. Geburts. u. Gynäk.*, 1905, lvi, 154.
- ⁴ Liepmann: *Handbuch der Frauenheilkunde*, 1914, ii, 182.
- ⁵ Davidsohn: *Klin. Woch.*, 1910, xlvii, 1013.
- ⁶ Lefquist: Quoted by Hartz.
- ⁷ Hartz: *Trans. Path. Soc.*, Philadelphia, November 26th, 1914.
- ⁸ Duggan, D. J.: *New England Journ. Med.*, January-June, 1930.
- ⁹ Solomons and Smith: *Journ. Obstet. and Gynaecol.*, 1923, xxx.
- ¹⁰ Phillips, M. H.: *Ibid.*, 1911, xx.
- ¹¹ Fleurent: *Bull. Soc. d'Obstét. et de Gynéc. de Paris*, May, 1933.
- ¹² Lynch and Maxwell: *Pelvic Neoplasms*, 1931.
- ¹³ Friedlander, B.: *Journ. Amer. Med. Assoc.*, November 8th, 1930. (Discussion on paper, "Malignant Chorionepithelioma Uteri," by Schmitz and Hueper.)

According to S. J. J. Leroux (*Thèse de Paris*, 1934, No. 307) undulant fever is not uncommon in Paris, but often escapes recognition. It is usually contracted by slaughterers and butchers who come in contact with sheep from the Mediterranean district. The other chief sources of contamination are raw goat's milk and cheese. Undulant fever in Paris does not assume any special clinical form, but complications are rare and the prospect of recovery is excellent. As regards treatment, novarsenol, vaccine treatment, and microbial extracts in the form of melitin, endoprotein, or endoglobulin prepared from *Br. abortus* should be employed. Prophylaxis should be carried out by vaccination in infected areas, boiling the milk, and the creation of co-operative stores for the sale of milk and cheese with a sanitary guarantee. The thesis contains the histories of twenty cases in patients aged from 10 to 49.