

given either a progestogen or a natural estrogen alone. That there is a significant relationship between oral contraceptives and thrombosis appears to be fairly well accepted and therefore the same must be true, to some extent, with regard to the Budd-Chiari syndrome.

Although the evidence is circumstantial in nature, it seems a reasonable conjecture that one or both of the factors discussed were to some extent operative in the pathogenesis of thrombosis in our case.

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Yesterday's Medicine

THE SIGNIFICANCE OF A SMALL AMOUNT OF SUGAR IN THE URINE

Every physician who makes it a practice to examine the urine of his patients will find frequently, and often quite unexpectedly, a small amount of sugar in the urine. At once he is confronted by the question, what is the meaning of this discovery? Has the patient a mild diabetes? The answer is of more than academic interest, for upon the proper answer depends the comfort and welfare of the patient. If this symptom is an interesting but innocent abnormality, then it is an injustice to force the patient to undergo the inconvenience of a rigid diet. If the patient truly has a mild diabetes, then it is unpardonable neglect to allow him to continue unguided and unwarned. — L. Hamman: *Canad. Med. Ass. J.*, 9: 961, 1919.

Allergic Reactions:

Patent blue is an aniline dye, Alphazurine 2G, used to identify lymphatics before cannulation at lymphangiography. Allergic reactions to the administration of the dye are extremely rare. Only a few references are to be found in the current literature. Hepps and Dollinger¹ described cardiac arrest following its use in a patient with burns, while Kopp² reported two cases of allergic reaction following injection at lymphography. However, at the International Symposium on Lymphology held in Zurich in July 1966³ another 12 cases were described during the discussion on complications of lymphangiography. On the basis of a large series of 16,000 it was suggested that the probable incidence is about 1 in 1000.

This communication describes two further cases.

CASE 1

An 18-year-old youth, who complained of fever and general malaise for five months, was found to have swelling of the cervical glands on the right side. Biopsy of one of these nodes confirmed a diagnosis of Hodgkin's disease and the patient was treated with radiotherapy. Symptoms recurred one month after the cessation of therapy and this time they were accompanied by epigastric pain. He also suffered from allergic rhinitis for which he was receiving treatment by desensitization.

Examination at this time revealed a temperature of 103° F., blood pressure of 110/70, pulse rate of 84 and a palpable node in the left supraclavicular fossa but no other relevant masses. It was decided to perform a lymphogram.

Ten minutes after the injection of 0.5 ml. patent blue dye into the webs

between the first two toes of both feet he developed hives, began to shiver and became cold. Within a further 10 minutes his lips became swollen, and he had difficulty in swallowing. At this time he was pulseless and the blood pressure was barely recordable.

He was treated with diphenhydramine hydrochloride (Benadryl), 3 ml. intravenously, adrenaline 1:1000, 1 ml. subcutaneously and hydrocortisone sodium succinate (Solu-Cortef), 100 mg. intravenously. An intravenous drip was set up and a further 50 mg. of hydrocortisone sodium succinate was given. After 30 minutes his blood pressure was 100/60 and pulse 92 and he was well enough to be returned to the ward. The patient made a complete recovery from the reaction.

CASE 2

A 66-year-old woman was admitted in December 1966 with bilateral femoral vein thrombosis. Intravenous pyelography demonstrated a non-functioning right kidney due to obstruction of the ureter. A mass was palpable in the right lumbar region. At laparotomy a large right-sided retroperitoneal tumour was found obstructing the ureter and invading the mesentery of the small bowel. Biopsy proved this mass to be a lymphosarcoma. Treatment by radiotherapy relieved the ureteric obstruction and the mass disappeared. Afterwards the patient had been treated with chlorambucil and further radiation.

She was later readmitted because of small bowel obstruction and ascites. Lymphangiography was carried out at this time. The first interdigital webs of both feet were infiltrated with idocaine 2% followed by 0.25 ml. of patent blue injected into each web. After 20 minutes the patient complained of feeling unwell, cold and shivery. It was noticed that her face

D. J. SINCLAIR, F.R.C.P.[C]* and
F. A. PERERA, F.R.C.P.[C],†
Victoria, B.C.

Following Patent Blue Dye Injection

was slightly swollen. On the flexor surface of the arms and in the creases at the elbows, there were wheals which at their centre had a blue coloration quite distinct from the rest of the skin. After a further 20 minutes the patient felt better and the skin lesions began to regress, so that at the end of two hours only the discolouration persisted. This too had disappeared after 12 hours, and the patient felt no ill effects from the procedure.

A scratch test was performed on this patient three days afterwards, using a dilution of the same dye, but no further local reaction could be elicited.

DISCUSSION

The reactions produced in both of these patients were similar to those described by Kopp. In the first case no local anesthesia was used, so that the reaction could have resulted only from the patent blue. In addition, the patient had a history of allergy treated by desensitization. In the second case the reaction could have resulted from either lidocaine or patent blue. The blue discolouration in the wheals was considered initially to indicate that the dye was the primary cause of the reaction, especially since allergens in the bullae produced by such allergens as antipyrine and phenolphthalein have been detected by others.⁴ However, it has also been shown that Evans blue given intravenously immediately before an injection of antigen in a previously sensitized patient produces a bluish discolouration at the site of the sensitizing antibody injection.⁵

The discolouration in the second case therefore cannot be considered as indicative of specific allergy to patent blue. This same patient, how-

ever, had an abdominal paracentesis when the same local anesthetic was used, three days after the lymphogram, and there was no reaction, proving that lidocaine was not the cause.

The Alphazurine 2G in both cases came from the same stock bottle; different freshly prepared solutions were used. These solutions were prepared by the same pharmacy by mixing 1.1 g. Alphazurine 2G with 10 ml. distilled water to produce an 11% solution. This was then autoclaved at 115° C. for 30 minutes. Similar solutions have subsequently been used on 12 other patients, without reactions.

The detection of sensitivity is not easy and often impossible. There is rarely a specific history of sensitization, and in the above two cases no history of previous contact with patent blue could be found. Aniline dyes, however, are used extensively in the fabric and carpet industries, so that contact with their products and subsequent sensitization is not necessarily uncommon.

Skin testing may prove falsely negative or, alternatively, positive enough to produce a systemic reaction.

A scratch test was carried out in the second patient and proved to be negative. This is of some significance, since it reminds one that such forms of testing are not entirely reliable, although undoubtedly less hazardous than intracutaneous injection.

It is also of interest that of the five patients with allergic reaction reported in detail two suffered from Hodgkin's disease and a third from lymphosarcoma. The immunological peculiarities of Hodgkin's disease are well recognized; in particular a marked cutaneous allergy is present, especially in the acute phase. This phenomenon can also be present in the terminal phases of lymphosar-

coma and other lymphomas.⁶ Since the two cases reported here fall into each of these categories, skin testing would have been expected to be of little value and indeed proved to be so in the second case. Because a large proportion of the patients submitted to lymphangiography do suffer from these conditions, the allergic phenomenon referred to throws some doubt on the value of preliminary skin testing to detect sensitivity.

One alternative is to identify the lymphatic vessels without dye, as suggested by Maddison.⁷ This method, however, to most of us seems extremely difficult. Another alternative would be to use a different dye, but all those available are of a similar chemical structure.

Therefore one must recognize that there is a very slight risk involved in using an aniline dye, which must be added to the already long list of complications reported of lymphangiography. Preliminary skin testing may help to detect those sensitive, but the limitations of this method must also be acknowledged.

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*Associate Radiologist, St. Joseph's Hospital, Victoria, British Columbia.

Reprint requests to: Dr. D. J. Sinclair, Radiodiagnostic Department, St. Joseph's Hospital, Victoria, British Columbia.