The thrombotest method is relatively insensitive to a reduction in Christmas factor, but correlates well with the one-stage prothrombin time.

For the routine clinical laboratory the one-stage prothrombin time as a means of controlling therapy is perhaps still the method of choice, by virtue of its technical simplicity.

I thank Professor M. Maizels and Dr. Rosemary Biggs for their most helpful advice and criticism. The "dindevan" used in the study was supplied by Evans Medical Supplies Ltd.

REFERENCES

- Allington, M. J. (1958). *J. clin. Path.*, **11**, 62.
 Bachmann, F., Duckert, F., and Koller, F. (1958). *Thromb. Diath. haemorrh. (Stuttgart)*, **2**, 24.
 Bell, W. N., and Alton, H. G. (1954). *Nature (Lond.)*, **174**, 880.
 Biggs, R. (1956). *Brit. J. Haemat.*, **2**, 412.
 — and Douglas, A. S. (1953a). *J. clin. Path.*, **6**, 15.
 — (1953b). *Ibid.*, **6**, 23.
 — and Macfarlane, R. G. (1957). *Human Blood Coagulation and its Disorders*, 2nd ed. Blackwell, Oxford.
 Denson, K. W. (1958). *Brit. J. Haemat.*, **4**, 313.
 — (1961). *Acta Haemat. (Basel)*, **25**, 105.
 Douglas, A. S. (1955). *Brit. med. Bull.*, **11**, 39.
 Duckert, F., Flückiger, P., Matter, M., and Koller, F. (1955). *Proc. Soc. exp. Biol. (N.Y.)*, **90**, 17.
 Greig, H. B. W. (1959). *Lancet*, **2**, 25.
 Hicks, N. D., and Bonnin, J. A. (1959). *Brit. J. Haemat.*, **5**, 194.
 Hörder, M. H. (1958). *Thromb. Diath. haemorrh. (Stuttgart)*, **2**, 170.
 Hougie, C., Barrow, E. M., and Graham, J. B. (1957). *J. clin. Invest.*, **36**, 485.
 Loeliger, E. A., Esch, B. van der, Haar, C. C. ter, Romeny-Wachter, C., and Booi, H. L. (1960). *Thromb. Diath. haemorrh. (Stuttgart)*, **4**, 196.
 Michaelis, L. (1931). *Biochem. Ztschr.*, **234**, 139.
 Naeye, R. L. (1957). *Proc. Soc. exp. Biol. (N.Y.)*, **94**, 623.
 Owren, P. A. (1959). *Lancet*, **2**, 754.
 — and Aas, K. (1951). *Scand. J. clin. Lab. Invest.*, **3**, 201.
 Sise, H. S., Lavelle, S. M., Adams, D., and Becker, R. (1958). *New Engl. J. Med.*, **259**, 266.
 Telfer, T. P., Denson, K. W., and Wright, D. R. (1956). *Brit. J. Haemat.*, **2**, 308.
 Toohy, M. (1958). *J. clin. Path.*, **11**, 56.
 Verstraete, M., and Vandenbroucke, J. (1956). *Acta med. scand.*, **155**, 37.
 Walker, W., and Hunter, R. B. (1954). *Nature (Lond.)*, **173**, 1192.

MULTIPLE PAINLESS GLOMUS TUMOURS

BY

J. T. HUESTON, M.S., F.R.C.S., F.R.A.C.S.

Assistant Plastic Surgeon, Royal Melbourne Hospital

While still regarding the whole range of glomus-celled anomalies as variants on the same theme, it seems both reasonable and practical to delineate certain clinical types which correspond to recognizable variants in the histological structure, and require quite different treatment.

It is becoming clear that two forms of glomus anomaly occur, neither being a true neoplasm. The first is the solitary painful lump which is an organoid malformation or hamartoma, the other being the diffusely distributed multiple painless lesions which are more telangiectatic in nature.

Two cases showing a familial relationship are reported here to indicate the differences in this second group from the typical painful glomus tumour.

Case 1

A woman aged 24 sought medical advice because of the progressive enlargement of a lesion on the dorsum of the right hand. This lesion had appeared six or seven years previously as a soft, slightly raised lump beneath the skin, but in the past two years had become bluish in colour, and

had doubled its size in the past six months. Several dilated veins adjacent to the lesion had been present for a few months, and her main concern was the unsightly appearance of the lump; she also had a mild curiosity regarding its nature. At no time had it been painful or tender.

Examination revealed, in the centre of the dorsum of the right hand, a bluish dome-shaped mass, 1.5 cm. in diameter, soft in texture, compressible without complete obliteration, non-pulsatile, and of the same temperature as the surrounding skin to rough clinical tests. Three distended veins passed distally and one proximally from the lesion. A separate small mass 3 mm. in diameter, with similar features, was present just under the skin, about 3 cm. proximal to the main mass. The lesion was thought to be an unusual variety of arteriovenous communication, and local excision was advised.

At operation the dermis was closely adherent to the surface of the central vascular mass, which consisted of three or four large tortuous cavernous masses from which several veins radiated both up and down the dorsum of the hand and obviously having the highest point of venous pressure at the mass rather than distally at the fingers. Only one small artery entered the mass on its deep aspect.

Histologically the mass consisted of several groups of large blood spaces surrounded by collars of fairly regular small glomus-type cells, which were sometimes several layers deep but often only one or two cells deep (Figs. 1 and 2). In some of the cellular areas a mucoid material was present between the cells. The lobulated blood spaces were well separated from the surrounding fat.

On further questioning the patient stated that several small bluish spots in the skin of her arms, legs, and breasts had begun to appear after the age of 8 years. The spots

FIG. 1.—Case 1. Photomicrograph of lesion from hand, showing large vascular spaces lined by glomus-type cells. (×122.)

FIG. 2.—Case 1. Higher-power photomicrograph of glomus cells in trabeculae of lesion. (×540.)

have appeared roughly in episodes, when four or five may have become visible over a few months but nothing more for some years. Beginning as tiny pin-point spots, these slowly enlarged, and, on becoming 3 to 4 mm. in diameter, took on a low dome-shaped contour. Most of these lesions were single, but several appeared as small clusters; one in particular she related to the site of a Mantoux injection on the right forearm.

There has never been any spontaneous or induced pain in these lesions or any symptoms produced by change in the surrounding temperature.

Case 2

This patient, a man aged 26, is the only brother of the previous patient. In the same position, on the dorsum of his right hand, there is a raised bluish lump 1 cm. in diameter and identical clinically with the lesion removed from the same area on his sister's right hand (Fig. 3). This lesion had been noticed for over 10 years, and there was a history of the skin in this region having been punctured by a nail at football many years before, but no scar could be detected.

On the right upper arm there was a cluster of several blue spots ranging from 1 to 3 mm. in diameter, and related by the patient to his vaccinations in this area some years previously, but no scar was visible at this site (Fig. 4). On both arms and both legs, and on the back of the trunk and buttocks, many similar lesions were present. These ranged from tiny impalpable but completely collapsible areas clearly composed of large blood lakes to raised palpable masses irregular in outline and only partly compressible. Two such bluish clusters of tissue which had been present on the back of the left thigh for five years were regarded by the patient as "just varicose veins." There had been no pain, tenderness, or temperature changes associated with any of the lesions.

FIG. 3.—Case 2, brother of Case 1. Raised bluish compressible lump on dorsum of right hand clinically identical with lesion excised from his sister.

FIG. 4.—Case 2. Cluster of typical lesions on outer aspect of right arm.

It was impossible to count the total number of lesions present on either of these patients because the range passed smoothly from large to barely visible, and presumably to the microscopic which may later become visible.

Both brother and sister are emphatic that their late father had, for as long as they could remember, a raised bluish lump on the dorsum of the right hand similar to their own, although smaller in diameter.

Discussion

Since the classical paper of Masson (1924) first related the extremely painful subcutaneous nodules, which had been described by Cheselden as long ago as 1740, to the neuro-myo-arterial glomus apparatus, several hundred such tumours have been reported. It is possible to divide these reports into three clinical groups.

1. Solitary glomus tumour: this being the commonest presentation with a very painful nodule, usually on an extremity, associated with radiating pain triggered by touch or temperature change, sometimes with demonstrable changes in the skin circulation of the whole limb and completely cured by surgical extirpation.

2. Multiple painful glomus tumours: rarely more than three or four in number, but each presenting the same features as a solitary glomus tumour. As Rowntree (1952) has indicated, these are always well localized to a circumscribed area of the body. In such a local grouping the tumours may also occur in deeper tissues such as beneath the deep fascia (Rowntree, 1952) or within a bone (Bergstrand, 1937). Both clinically and histologically these tumours are identical with the solitary glomus tumour, and seem merely to represent a regional tendency to the formation of this lesion.

3. Multiple painless glomus tumours: in which the lesions are numbered in dozens, are widely distributed, and give rise to no symptoms (Weidman and Wise, 1937). Both clinically and histologically these lesions appear to be primarily vascular in origin, and at the other end of the scale from the much more cellular, very painful glomus nodules. While it is realized that exceptions do occur, it is felt that such a generalization is both warranted and useful. A case such as that of Eyster and Montgomery (1950), in which two painful lesions were present as well as several dozen painless lesions, probably represents, as those writers suggest, a transitional form between the two extremes of structure.

It is now generally accepted that the nature of the solitary glomus tumour is that of an organoid malformation or hamartoma, in which the masses of glomus cells and nerve endings aggregated about the vascular spaces roughly simulate the structure of the normal glomus. Three histological gradings are recognizable, depending on the relative proportions of glomus-cell proliferation to the size of the vascular lumina. Thus we find lesions with normal proportions, others with relatively more cellular structure, and finally those predominantly vascular in structure. No definite correlation has been attempted between the severity of symptoms and the histological structure. Slepian (1944) compared the histology of a painful glomus tumour with that of a painless glomus tumour from the same patient, and indicated that the lesion giving rise to symptoms was the more cellular. In a series such as that reported by King (1954) it is of interest not only that the multiple lesions were all vascular but that several of the vascular lesions were painless, whereas all the cellular lesions were painful.

The present cases indicate that, since the multiple painless lesions are of the vascular type, this correlation is probably significant. However, there is no explanation why a solitary cellular painful malformation should occur in one person while multiple vascular painless lesions appear in another. It is probable that two quite different factors are operating to produce these two groups of cases. The solitary cellular lesion represents an isolated malformation occurring sporadically and quite accidental in origin. The multiple vascular telangiectatic type of anomaly may be genetic in nature as suggested in this instance, where brother and sister are similarly affected; and they described an identical lesion on their late father. The diffuseness of the distribution of these telangiectatic lesions favours the probability of such a general somatic factor being responsible. The progressive appearance over several years is still consistent with our knowledge of glomus-cell production, this being normally a post-natal development, and may in fact occur anywhere from aggregation and hyperplasia of local spindle cells normally in and around any blood-vessel walls. The possible initiation of some lesions by local trauma is suggested in the history of both cases reported, and it may be significant that each injury involved a puncture wound, by needles and once by a nail.

Thus it seems that the basic abnormality in these patients is vascular, the occurrence of telangiectases being distinguished by a hyperplasia of glomus-type cells irregularly scattered in the walls. It is suggested that such multiple painless lesions can be separated from the solitary lesion, wherein cellular proliferation is more prominent, and that nearer-to-normal glomus structure is reproduced both structurally and functionally.

Summary

Glomus-cell development is a normal postnatal event, and abnormalities of this process may result in a range of lesions showing different degrees of glomus-cell hyperplasia and different proportions of vascular to cellular components in these lesions.

While the usually solitary cellular painful glomus "tumour" or hamartoma is well recognized, the multiple, more vascular or telangiectatic type of painless lesions is not.

Two cases, those of a brother and sister, are reported with multiple painless glomus lesions, and the significance of these lesions is discussed in relation to the present concepts of glomus-cell abnormalities.

REFERENCES

- Bergstrand, H. (1937). *Amer. J. Cancer*, **29**, 470.
 Cheselden, W. (1740). *Anatomy of the Human Body*, 5th ed., p. 136. London.
 Eyster, W. H., jun., and Montgomery, H. (1950). *Arch. Derm. Syph. (Chicago)*, **62**, 893.
 King, E. S. J. (1954). *Aust. N.Z. J. Surg.*, **23**, 280.
 Masson, P. (1924). *Lyon chir.*, **21**, 257.
 Rowntree, T. (1952). *Brit. J. Surg.*, **40**, 142.
 Slepyan, A. H. (1944). *Arch. Derm. Syph. (Chicago)*, **50**, 179.
 Weidman, F. D., and Wise, F. (1937). *Ibid.*, **35**, 414.

A booklet, *Notes on W.V.S. Health and Hospital Work*, gives a bird's-eye view of the work done by the Women's Voluntary Services in hospitals (canteen work, shopping, library services, work in out-patient departments, and staffing telephone trolleys), in the blood transfusion, mass radiography, and hospital car services, and in their work for sick and handicapped people in the community. There is a list of useful books and an index. Inquiries should be sent to W.V.S. Headquarters, 41 Tothill Street, London S.W.1.

SYNDROME OF COLOBOMA WITH MULTIPLE CONGENITAL ABNORMALITIES IN INFANCY

BY

HARRY ANGELMAN, M.D., M.R.C.P., D.C.H.

Paediatrician, Warrington General Hospital

During the past ten years coloboma of the eyes has been noted in four infants in our paediatric wards, and in every case it has been accompanied by other congenital abnormalities, particularly affecting the brain and heart. The main features of these cases are here described.

Case 1

A male infant was admitted to the Warrington General Hospital when 12 days old, with a history of increasing jaundice since birth, slowness in taking feeds, and general weakness. He had been born at home, a forceps delivery complicated by intrapartum haemorrhage. The birth weight was 7 lb. 8 oz. (3,400 g.). The mother's pregnancy was normal. There are two other children, both normal.

On admission he was jaundiced and a large cystic mass could be palpated, filling the lower part of the abdomen. Bilateral colobomata in the "typical" position were noted, involving the choroid, retina, and iris of both eyes. A systolic murmur could be heard to the left of the sternum. He had to be tube-fed. He was transferred to the neonatal surgical unit at Alder Hey Children's Hospital, where an intravenous pyelogram showed a normal right kidney but no excretion of dye on the left side. Laparotomy revealed the presence of an enormous hydronephrosis on the left side, compressing the inferior vena cava and the common bile-duct, this being the cause of the jaundice. Nephrectomy was performed and the jaundice gradually faded. It soon became evident that he had a severe degree of cerebral palsy. Head control and sitting were much delayed; both arms were spastic and his legs were small, weak, and hypotonic.

At the time of writing, aged 5 years, he could not assume the sitting position unaided, nor could he maintain his weight on his legs for more than a few seconds. He was speechless and his comprehension was almost negligible. He was able to see objects which were close to him, but vision was poor and there were constant searching movements of his eyes. He could pick up large objects but dropped them immediately. His head circumference was only 18½ in. (47.5 cm.). The cerebrospinal fluid was normal. Cardiac enlargement was present with cyanosis of the lips, fingers, and toes. There was a systolic thrill and murmur, maximal in the second left intercostal space. The E.C.G. showed right ventricular dominance and x-ray examination and cardioscopy showed right ventricular enlargement, concave pulmonary arc, and diminution of pulmonary vascular markings, these findings being indicative of pulmonary stenosis. He had difficulty in swallowing solid food and severe nutritional anaemia occurred on two occasions. Respiratory infections occurred and also large faecal accumulations in the rectum. His scrotum was cleft—this, together with a small penis, giving an almost hermaphrodite appearance.

Case 2

This patient was born in June, 1955, at the Warrington General Hospital, a full-term normal delivery, his birth weight being 8 lb. 15 oz. (4,055 g.). The pregnancy had been normal and there was one other child, aged 3 years, in good health. A number of congenital abnormalities were noted after birth, including talipes equinovarus of the left