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ROYAL SOCIETY OF MEDICINE—SECTION OF LARYNGOLOGY

President: N. ASHERSON, F.R.C.S.

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Management of Epistaxis in Familial Hæmorrhagic Telangiectasis

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C. L. JOINER, M.D. (*London*) said: When I came to review the patients whom my E.N.T. colleagues had asked me to see for them I realized that many were of outstanding medical interest. Of course, these were the exceptional cases for them: the few who didn't respond in the usual way to local hæmostatic measures. So you will forgive me if when I discuss them I seem to dwell on the most serious cases, and the most unusual. I should like to discuss them under two headings—their immediate management and their final diagnosis and treatment.

General. All people who have bled severely and especially those in whom this bleeding has been from the nose are severely distressed. There is no better drug than morphine in allaying their alarm and sedating them. They are also more vulnerable to infection, especially in this case to respiratory infection consequent upon the inhalation of blood; an antibiotic should always be given, and continued for five days after all bleeding has ceased. It is essential to have clear ideas about the indications for transfusion; they have been long established as a heart rate sustained at over 100 beats per minute, or a rising heart rate; a systolic blood pressure remaining at below 100 mm. Hg, or a progressively falling blood pressure; and a hæmoglobin level of less than 40 per cent. (5 g./100 ml. blood). These are absolute indications for transfusion in the face of hæmorrhage but other circumstances may constitute relative indications, and may combine to necessitate transfusion without the fulfilment of these absolute indices.

If transfusion is decided upon, then it should be given with the double intention of restoring the blood volume and encouraging the cessation of bleeding. For this reason freshly drawn blood is to be preferred, and may have to be drawn in such a way as to retain its platelets. It should be emphasized that only in the most disastrous hæmorrhages should the total volume transfused exceed two pints (1,080 ml.) of blood. It has been clearly shown that giving very large volumes of stored blood which is normally poor in platelets may prolong bleeding and do more harm than good. If the patient is in a dehydrated and collapsed condition, then infusion of a repair solution other than blood may be continued so as to ensure an adequate urinary output.

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Hypertension. One of the most important causes of continuing epistaxis is hypertension. It is essentially an arteriolar disease but the effect of the changes is to raise the pressure in the arteries, and so cause vessels already damaged, particularly by atheroma, to rupture. Once ruptured the increased pressure may interfere mechanically with the hæmostatic processes, and so lead to continued bleeding. Usually the diagnosis is clear enough. The patient may be a known hypertensive; it may be that the high diastolic pressure is sustained despite blood loss. But sometimes it is far from obvious, and for this reason careful inspection of the retinal arterioles is an essential part of the clinical examination. Evidence of left ventricular hypertrophy may also exist, although this may be masked in the elderly by coincident emphysema.

If it is concluded that a raised diastolic pressure is an important factor in continuing epistaxis, then it must be reduced. In general this is only dangerous in the elderly or those in whom the blood pressure has been long sustained at high levels. If a patient continues to bleed severely then these risks should be accepted, and the pressure reduced so that the diastolic level does not exceed 100 mg. Hg. I have found inversine (mecamylamine hydrochloride) to be the most useful drug in reducing the blood pressure rapidly. Because of its side effects, especially constipation, it is not ideal for long term administration. A better drug is ismelin (guanethidine) but its effects are much slower in onset. For this reason it is better to start with mecamylamine and continue with ismelin when the crisis has passed.

The combined effects of reducing the blood volume and lowering the blood pressure may precipitate oliguria or even anuria in kidneys already damaged either by nephritis or hypertension. Because of this, close observation must be made of the urinary output and the blood urea. If oliguria occurs, then dehydration should be corrected, and thereafter only 600–1,000 ml. of fluids be given in each 24 hours until the urinary output recovers. During this time 2–3,000 cals. daily must be supplied. This is best effected by an infusion of concentrated glucose solution directly into the inferior vena cave through a fine polythene tube passed upwards through the femoral vein. Whilst it is being given extra vitamins, particularly of the B group are required and may be supplied by 5 ml. of parentrovite intravenously daily. As soon as the urinary volume begins to increase fluids may be given by mouth and at this time close watch must be kept upon the blood electrolytes.

Continued treatment of blood pressure may be an essential prophylactic measure to prevent further epistaxis. Cases must be assessed on their merits, but in severe hypertension the most generally useful conbination of drugs at the moment is chlorothiazide and ismelin.

Bleeding Diseases. Next I should like to speak briefly about abnormalities of blood coagulation. The commonest by far of these is iatrogenic; those patients who are being given anticoagulant substances therapeutically.

Here is a list of preparations currently in common use, and their antidotes. In the presence of epistaxis the antidote should be given and the risks of thrombosis accepted.

Nose bleed is a frequent complication of other naturally occurring blood dyscrasias. These may be divided into those in which there is a reduction in blood platelets, and those in which the abnormality lies in the protein substances

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concerned with blood coagulation. They should always be detected provided that a full blood picture, including platelet count is made, and provided that bleeding, clotting, thromboplastin generation and prothrombin times are appropriately measured, and the tourniquet test observed.

Conditions in which platelets may be reduced include the leukæmias, especially the acute group, and in myelomatosis and the myelo-aplastic conditions. They are selectively reduced in thrombocytopenic purpura. These conditions may all be treated in an emergency by the transfusion of platelet-rich fresh whole blood. It must be collected and transfused through silicone lined needles and tubing and stored in plastic receptacles.

TABLE 1

Trade Name	Approved Name	Antidote
Heparin	Heparin	Intravenous protamine sulphate
Dicoumarol	Dicoumarol	Intravenous vitamin K Oxide
Tromexan	Ethyl biscoumacetate	
Dindevan	Phenidione	
Marevin	Warfarin sodium	
Sinthrome	Nicoumalone	

In some cases of essential thrombocytopenia platelet antibodies are present; in these steroid hormones may also be useful. In others splenectomy may be necessary. Specific chemotherapy is occasionally useful as a prophlactic measure in preventing nosebleeds in the chronic leukæmias.

Severe epistaxis may also occur in polycythæmia rubra vera. Its mechanism is often not apparent, but relief may paradoxically be obtained by venesection so as to reduce the packed cell volume (PCV) to less than 50 per cent.

Epistaxis and purpura are uncommon, but by no means unknown, in coagulation defects. More and more of these conditions are being identified exactly, and an already difficult subject grows daily more complex. An excellent simple and authoritative account is contained in M.R.C.Memorandum No. 32 (1955).

Identification depends upon specialist investigation, but may be suspected when there is a family history of the disease, and a lifelong tendency to bleed. Specific remedies are available for some of the conditions, but in an emergency bleeding can usually be controlled temporarily by the transfusion of freshly drawn whole blood.

Capillary Diseases. Purpura and epistaxis may also occur in other diseases affecting the capillaries and so increasing their fragility. Direct toxic effects are believed to be the cause of the epistaxis which may herald or accompany the specific fevers, particularly measles and typhoid fevers. Nose bleeding may be troublesome in the early stages of smallpox, particularly the malignant form preceded by the astacoid rash, and during the second week of Weil's

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disease these incidents are rarely severe or prolonged in our indigenous infections but may be severe in tropical infections, for example yellow fever and malignant malaria.

Capillary fragility is also increased in scurvy, now almost confined to the eccentric or insane. Drugs may also cause epistaxis, the classical example being the barbiturate "sedormid" one of whose actions is to damage capillary walls. These walls may also be weakened by protein withdrawal; this may be seen in the elderly as the result of long standing negative nitrogen balance, in association with so called senile ecchymoses. It may also occur with long continued steroid administration, and is common in Cushing's syndrome. Direct damage to capillaries may occur in certain auto-immune conditions, particularly systemic lupus erythematosus.

Congenital abnormalities of the capillaries also occur, and give rise to non-thrombocytopenic purpura (von Willebrand's disease). This is a lifelong affliction, and usually other members of the family are affected. It is best treated with small transfusions of freshly drawn whole blood.

Congenital abnormalities of the arterioles may also occur: we have already heard about hereditary hæmorrhagic telangiectasia: they may also occur in the Ehlers-Danlos syndrome. Arteriolar spiders may also appear during pregnancy, when they rarely bleed, and in cirrhosis of the liver, when they frequently do so. This is particularly dangerous because of the associated low prothrombin level and co-existent anæmia. They may also be seen in scleroderma, in which nose bleeds can be most intractable. Epistaxis may also occur in polyarteritis nodosa, and in the special subgroup described by Wegener (Wegener's granulomatosis) bleeding from the granulomas in the nose, sinuses, or ears is common.

Summary. In conclusion, may I say that in most cases where the bleeding does not stop, careful history taking and physical examination will give strong clues to the cause. Simple laboratory tests will nearly always allow certain diagnosis; and sedation, antibiotics and freshly drawn blood is always the treatment of choice in an emergency.

REFERENCE

Medical Research Council Memorandum No. 32. Macfarlane, R. G., and Biggs, R. (1955). London, H.M.S.O.

J. P. STEWART: I appreciate being asked to open this discussion on a subject which I know will provoke a lively debate. First of all may I congratulate the speakers on the excellence of their papers and the President on his choice of subject.

Frankly I am alarmed that ligation of the external carotid artery or one of its branches should be advocated for epistaxis. How many of us would allow our external carotid artery or one of its branches to be ligated for an epistaxis which I am convinced could be controlled otherwise? None of the six thousand cases I have told you about ever underwent such a ligation and I consider it quite unjustifiable. I would say that one might get away with it on a very odd occasion, probably once or twice in a lifetime, but if made a regular practice, it

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would undoubtedly get our speciality into disrepute. I concede of course ligation may be necessary in those cases of destructive tumours of the nasal cavities where bleeding in quantity arises.

I have used deep X-ray radiation for those obstinate cases which go on and on and on—when the blood loss is causing serious embarrassment to the patient and anxiety to the surgeon and when all the usual procedures for stopping an epistaxis have failed. The patients are given one single application of a dose of 750 rads. to the septal field and this of course is given with the nose firmly packed and the bleeding thus more or less temporarily controlled.

How does radiation act on the blood vessels to arrest the hæmorrhage? I show you a section of septal tissue removed three days after the cessation of treatment—this shows swelling and fissuring of the endothelial cells of the intima of a small blood vessel. The lumen is diminished and if the destructive processes on the endothelial cells continue then fibrin formation takes place replacing altogether or in part the available space for the blood. The tunica media is relatively unaffected but the tunica adventitia shows massive swelling with œdema.

The end results are shown in this next section. You can see very marked thickening of the walls of the blood vessels with narrowing and partial obliteration of the lumen space.

I have been able to collect the records of 27 patients treated in this way over the last 5 years. The bleeding ceased entirely within 24 hours and only in four was there a recurrence later within a 2 year period. Two of those cases suffered from familial telangiectasis which ultimately responded to the local injection of a sclerosing fluid while the other two were ordinary epistaxis patients—perhaps I should not have used the word "ordinary", for one of the cases was a barmaid with a high blood pressure and a high powered consumption of gin. No side symptoms such as dryness or discomfort in the nose occurred and no interference with the sense of smell has been complained of following radiation. I would confidently recommend this method of control to you in this type of case.

Perhaps I might end on a method of treating epistaxis which was used by some (not many I hope for the patient's sake) in the 1920s and this consisted in the local application of a nasal pack saturated with a solution of Stypven—the manufacturers' name for Russell's Viper Venom—it was reputed to act in a very salutary manner on the epistaxis. I remember particularly one case where I resorted to its use because do what I would, I could not get the bleeding to stop. After the application of this venom the bleeding certainly did stop, for good and for all. It must have been a pretty powerful reptile for when I removed the packs, which I was in no hurry to do, I found the nasal mucosa blackened and necrotic while there was a very pungent smell of snakes issuing from the nasal cavities—I never used it again.

J. Chalmers Ballantyne, F.R.C.S. (for A. Green, F.R.C.S), said: I have been asked by Mr. Anthony Green, my Radiotherapist colleague at the Royal Northern Hospital, to present very briefly a case of hereditary telangiectasia which he has treated for me at that hospital.

The patient was a woman of 46 when I first saw her at the end of 1958.

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Her mother, an aunt, and a sister had all suffered from repeated epistaxes and she herself had had them, from both sides of her nose, since she was 19 years old.

She presented the typical telangiectases on the face and lips and these also occurred on the tongue and other parts of the buccal mucosa.

The telangiectases occurred in well-defined areas of the septal mucosa on both sides. I treated these intermittently for 9 months; on several occasions

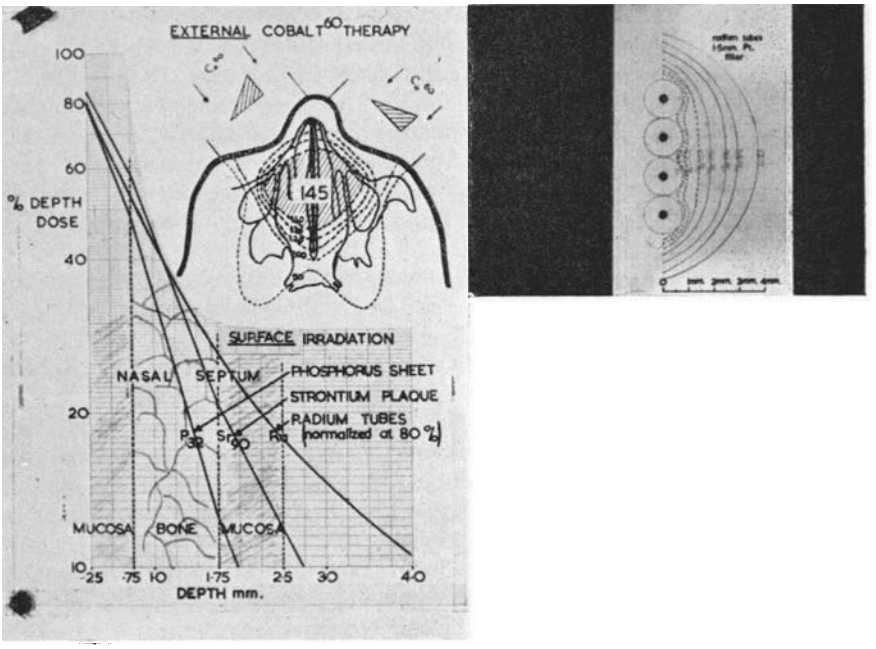


FIG. 1.

Control of Nasal Hæmorrhage by radio-therapy to the Septum.

by cauterization with the galvano-cautery and on one occasion by coagulation diathermy under general anæsthesia.

The bleeds however, continued and were often quite severe, and I referred her to Mr. Green in June 1959.

Several methods of radiotherapy may be used in these cases, and some of them are shown in the first illustration (Fig. 1). Cobalt 60 may be applied by external irradiation by means of the wedge technique which limits the radiation to the desired area.

Surface irradiation offers a more satisfactory alternative, and the graph on the left of the picture shows the depth-dose through the irradiated mucosa, the skeleton of the septum and the mucosa of the opposite side, of radio-active phosphorus, strontium plaque and radium tube (the right-hand picture shows the isodose curves for four radium tubes side by side).

It will be seen from the graph that there is a far more rapid fall of dosage

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with radio-active phosphorus than with either strontium 90 or radium, that is to say, the phosphorus is to be preferred to strontium or radium because its radiation is much more limited to the desired area.

The second illustration shows the methods of treatment applied in the present case (Fig. 2).

Radio-active phosphorus in polythene sheet was mounted on a thin perspex

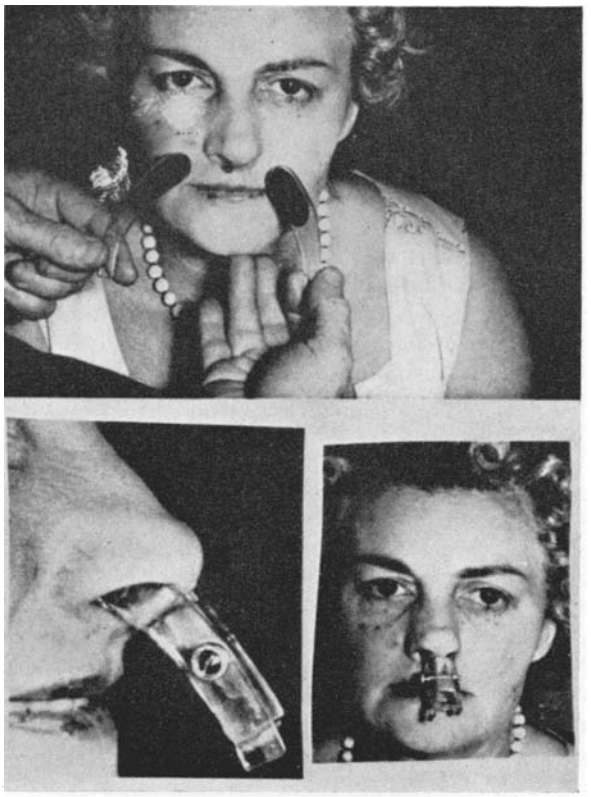


FIG. 2.
Treatment of Nasal Septum for Hæmorrhage using Phosphorus.

applicator, after the extent of the disease had been carefully assessed and drawn on graph paper. The applicators were applied to both sides of the septum and locked in position.

Only one single application of less than 1 hour's duration was given, and the patient has been very much better for $2\frac{1}{2}$ years. She has had no further bleeding at all from the right side, and it has been only slight and infrequent on the left.

PHILIP H. GOLDING-WOOD (*Maidstone*) said: I should like to comment on the use of trans-antral internal maxillary ligation and division in its several

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applications, namely in the acute severe bleed, in recurrent bleeding, and in hereditary telangiectasis.

In Acute Severe Bleeding. Appropriate arterial ligation is such an effective and time-honoured principle that the apparent reluctance of some to employ it when local measures fail speedily to control epistaxis is surprising. Various case reports refer to persistent re-packing etc. for periods up to three weeks, occasionally leading to nasal necrosis. Arterial ligation when ultimately employed relieved the situation, but it seems extraordinary that such circumstances should be allowed to arise.

It is generally practicable to decide whether bleeding is from ethmoidal or internal maxillary supply. Whether it is venous or not makes no practical difference.

We know ethmoidal arterial section is simple and effective. When this is inappropriate, trans-antral ligation of the internal maxillary is the ideal. The patient however, is often elderly, feeble or hypertensive and exhausted by blood-loss. In these circumstances external carotid ligation is preferable for it needs only 10 minutes under local anæsthetic. Even though the distal anastomosis may open up within a week, bleeding will be arrested just as well and more easily than by formal trans-antral ligation in possibly difficult circumstances. Bilateral ligation of any of these vessels is both feasible and safe.

Recurrent Bleeding. The difficulties arise in hypertensive patients when hypotensive therapy is unsuitable or ineffective, or when bleeding persistently recurs from inaccessible sites for no apparent reason. The problem is not the individual bleed but to avert its frequent recurrence.

External carotid ligation is useless. Surgical first principles require ligation immediately proximal to the site of bleeding. This generally arises from internal maxillary supply which can be ligated and divided just before it enters the nose by trans-antral approach.

The inexperienced may easily mistake a branch of this vessel for its stem, and this error renders the operation useless. Scissor dissection along the artery as it is held on a hook will quickly define both stem and branches, despite the considerable anatomical variations that occur. The arterial stem and major branches are separately clipped and the artery divided.

The clips and a few other instruments I use are made by Down Bros. and they greatly simplify the procedure. With familiarity this seldom requires more than 15 minutes.

Over the past ten years this operation has been used in 31 cases. It has markedly reduced both frequency and severity of bleeds and frequently has abolished them. Hypertensive cases particularly are liable to some recurrence after 2–3 years, when further division of septal and/or ethmoidal arteries has generally given further relief. Whilst these results are not perfect, the patients have been grateful for the marked relief obtained.

Hereditary Telangiectasis. No matter where it occurs, bleeding in hereditary telangiectasis is always surface. Furthermore, it is recurrent epistaxis alone that is the major cause of distress, and a not infrequent cause of fatality. The incidence of death from epistaxis being variously estimated from 4 per cent. (Fitz-Hugh, 1923) to 27 per cent. (Houser, 1934).

As Harrison points out, squamous epithelium seems a protective covering

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of considerable value. His ingenious use of œstrogens to promote squamous metaplasia of the nasal mucosa seems valuable. Although justified, the risks of gynæcomastia in males, endometriosis in females, hypercalcinæmia, salt retention or pituitary inhibition in both sexes, and the possible risks of carcinogenesis in long term treatment do impose considerable limitations in its use.

Various text-books state that arterial ligation has no place in this condition. The authors however, refer to external carotid ligation that offends surgical first principles. Ten years ago I found internal maxillary division gave definite improvement, although, by itself, it was disappointing. Endeavouring to increase the resistance of the nasal mucosa, zinc ionization was used 3 weeks after arterial ligation. Time and amperage were increased to induce some fibrosis in mucosa.

This combination has certainly helped. Most of the 19 cases so treated have been followed several years. Whilst bleeds have not been abolished, there has been substantial benefit from marked reduction in frequency and severity of bleeds, which mostly have been reduced to a mere show. Ten patients have been restored to full economic capacity, hitherto lost. This method is commended for further trial. Subsequent œstrogen therapy, if required, might enhance the value of both measures.

MR. J. SIEGLER said: I would like to ask the Speakers whether abnormal physical signs were found in the noses of those patients with severe Epistaxis they dealt with. In Liverpool we see many patients who are suffering from Epistaxis and when they have been fully investigated, we find that they are suffering from rhinitis, sinusitis or polypoidal changes of the mucous membrane over the turbinate bones. I have come to regard Epistaxis as a symptom of underlying disease, which ceases when the disease is dealt with.

ROYAL SOCIETY OF MEDICINE—SECTION OF LARYNGOLOGY

March 2nd, 1962

Discussion on Nasal Glioma

J. A. SEYMOUR JONES. In 1927, now 35 years past, at the Summer Meeting of this section held in this building, Guthrie and Dott of Edinburgh read a paper entitled "The occurrence of brain tissue within the nose: the so-called nasal glioma". They instanced two cases the first of which was undoubtedly a rapidly growing spongioblastoma multiforme which herniated in a most unusual fashion downwards into the nasal cavity and in spite of cerebral decompression, rapidly proved fatal. The second, however, appeared to fall into the group which we are discussing this afternoon.

Case History. The baby, Raymond, was referred to me at the Eye and Ear Hospital, Portsmouth, in *December, 1954,* by Dr. Moseley, our Pædiatrician, at the age of 1 month. His mother had noticed from birth some blockage of

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the left nostril and swelling of the left side of the nose (Fig. 1). There had been interference with breast feeding, which seemed to be due to the nasal obstruction, and persistent watering of the left eye. Apart from some asymmetry of the bridge of the nose, he appeared to be a normally healthy baby and there was

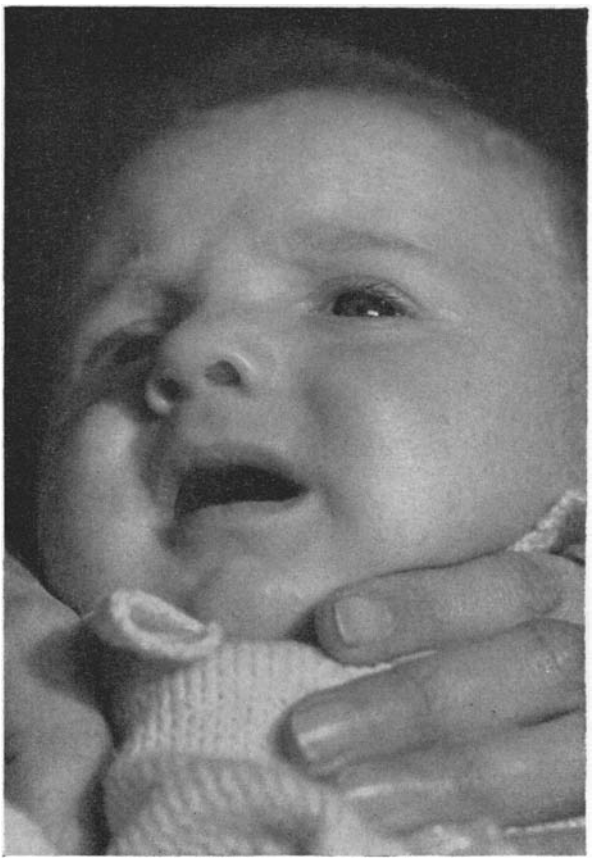


FIG. 1.
Patient aged 1 month.

no tumour visible on anterior rhinoscopy. A metal probe inserted into the left nostril passed easily into the nasopharynx. I made a tentative diagnosis of a fronto-ethmoidal dermoid. X-ray films showed some expansion of the left nasal cavity and thickening of the left nasal bone but no bony destruction.

Three months later, I was again asked to see the child because a fleshy polypus was now presenting at the left nostril and, therefore, I arranged to examine the baby under an anæsthetic and made a biopsy excision of the polypus, at the same time finding no abnormality in the post-nasal space. The polypus was firmly attached to the roof of the nose, clearly not arising from beneath the middle turbinate.

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Dr. Clay reported on the section: "A tissue of moderate cellularity covered by a thin layer of squamous epithelium, in places ulcerated. The tissue is composed of large and small cells in a fibrillary matrix: the fibrils stain purple with phosphotungstic acid hæmatoxylin and some of them are continuous with

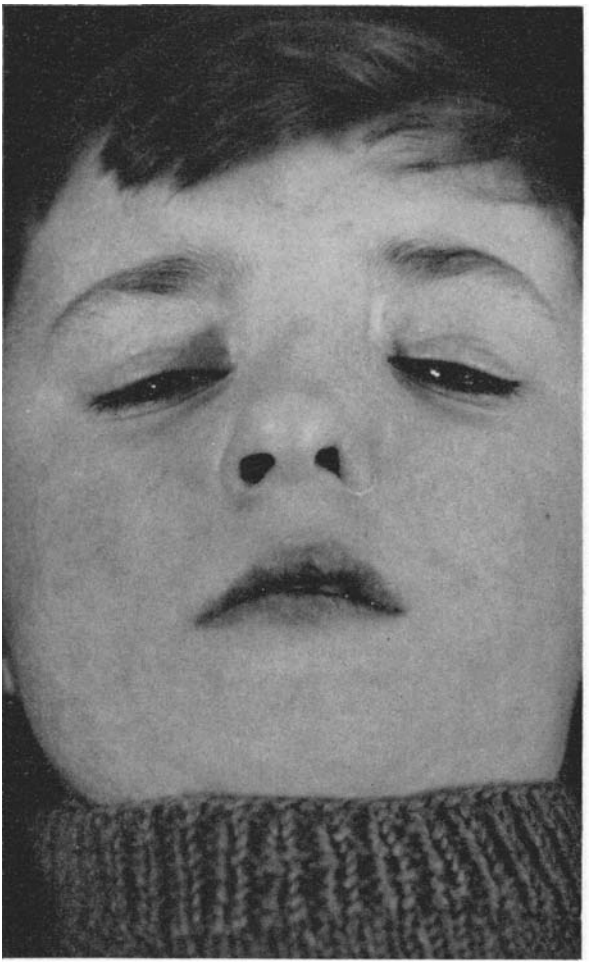


FIG. 2.
Patient aged 2½ years.

the cells bodies. The rest of the cells appear to be astrocytes but some of them may be ganglion cells. Conclusion: the polyp appears to be a nasal glioma."

Within 4 months the polyp had re-grown and was clearly visible in the left nostril. Mr. Mill kindly saw the baby for me and admitted him to St. Thomas's Hospital where our findings in Portsmouth were confirmed. Full pædiatric and neurological examinations revealed no further lesion and repeated

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X-ray studies failed to demonstrate with certainty any deficiency in the region of the left cribriform plate. The conclusion reached was that one was dealing with a slowly-growing glioma of the frontal lobe; that, is an astrocytoma which was unlikely to be radio-sensitive and moreover irradiation would probably have upset the normal growth of the facial bones. It was therefore decided that the baby should be kept under observation.

Three months later, however, no sign of an intracranial lesion had appeared and, therefore, in December 1955, Mr. Mill explored the nasal cavity by lateral rhinotomy. The tumour was found to be irregular in shape, of a reddish-grey colour and firmly attached by a broad base to the nasal vestibule from the inner canthus of the eye to the ala nasi and the atrium of the middle meatus. There was no ulceration, in fact the tumour appeared to lie underneath intact mucous membrane. Good exposure was obtained by partial removal of the expanded nasal processes of the maxilla. The growth was excised with scissors, great care being taken to avoid damage to the cribriform plate. The nasal cavity was of course very small and it was difficult to obtain a good view of the upper limit of the swelling which was pear-shaped and the narrow portion attached to the agger nasi. However, the upper limit appeared to be reached and the tumour excised in one piece without the necessity of having to do any work in the upper recesses of the olfactory cleft.

The specimen was examined by Dr. Pinniger who reported as follows: "An irregularly shaped piece of tissue 30 × 6 × 2 mms., the surface of which is smooth, grey or mottled-fawn in colour. The tumour consists of nasal mucous membrane and submucosa, including cartilage and mixed glands, showing slight chronic inflammation and contains areas of nervous tissue. The latter is not sharply demarcated from fibrous tissue but the individual cells show little variation in nuclear size. It is difficult on histological grounds to call this a glioma. The change appears more likely to be hamartomatous. No endothelial lined canal can be identified in any of the sections examined."

Immediately after the operation there was a watery discharge from the left nostril which was thought to be cerebrospinal fluid. Despite penicillin therapy the temperature rose sharply and the third post-operative day there was some neck rigidity. Lumbar puncture revealed purulent fluid, sterile on culture. The baby was treated with intramuscular streptomycin, sulphadiazine by mouth and intrathecal penicillin. The temperature abated and the neck rigidity disappeared. By the fourteenth post-operative day there was no evidence of cerebrospinal rhinorrhœa and he was discharged home.

He remained well until he was two years old, passing the normal milestones at the average age. He was walking at 18 months and talking in sentences at two years.

In *April, 1957*, at the age of two years and four months, he suddenly became drowsy and irritable and started to vomit and was admitted to the Infectious Diseases Hospital, Portsmouth, where he lapsed into a semi-comatose state.

Lumbar puncture showed turbid fluid containing pus cells. He was again treated with penicillin and sulphadiazine and intrathecal streptomycin. Two days later he developed twitching of the face and flaccid paresis of the right arm and he was transferred to the Neurosurgical Department at Great Ormond

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Street under the care of Mr. Wylie McKissock. X-ray films of the skull taken there showed suture diastasis indicative of raised intracranial pressure. It was thought likely that he had a left frontal collection of pus and accordingly the day after admission burr holes were made in the left frontal and left parietal regions without revealing any evidence of pus but exposing a brain which was congested and very soft. A portion of this brain was removed and later grew coagulase positive *Staphylococci*. Ventriculography was at the same time carried out and showed displacement of the ventricular system to the right.

It was considered that he had diffuse pyogenic encephalitis. He was treated with streptomycin for 9 days after admission together with penicillin and made a slow, steady recovery.

The question of whether he should have a frontal exploration in order to close the communication from his cribriform plate was considered but thought not to be advisable unless he had further trouble.

Later the same month he was transferred to Mr. Mill's care at St. Thomas's Hospital, when he looked well (Fig. 2), had a slight right facial paresis, and flaccid paralysis of the right arm and leg. He made a very considerable degree of recovery from his hemiplegia and was discharged home. Since that date he has suffered several attacks of otitis media and upper respiratory tract infections and finally in October last year his tonsils and adenoids were removed and he made an uninterrupted recovery.

When classifying congenital cerebral herniae it is customary to speak of the associated condition where there is a deficiency of the skull, as cranium bifidum, a condition similar to spina bifida which was considered by Ingraham and Metson to occur at least six times as commonly as a cranial lesion. Houll stated that the incidence of cranium bifidum was in the region of one in 3,500—4,000 births. Both conditions are associated with protrusions of portions of the nervous system and its protective meningeal covering.

Three types of cephalocele are usually described, that is meningocele, encephalocele, hydrocephalocele, but Duke-Elder suggested that the three are really varieties of a single entity and that nearly all cephaloceles contain brain substance. They are often extremely atrophic through pressure changes and cyst formation, the pia-arachnoid being usually unrecognizable. McGillicuddy was of the same opinion and suggested the term encephalomeningocele for all hernias of the brain. They may be situated posteriorly in the occipital region and, much less frequently, anteriorly where the sub-division is made into those of the sinciput, and those of the basis cranii.

Sincipital encephalomeningoceles are found at the inner angle of the orbit or root of the nose and resemble those of the occiput in consisting of visible external tumours, whereas the basal forms which protrude into the nasal cavity or nasopharynx are not so readily evident.

The most detailed classification of the sincipital and basal forms is given by Gisselsson.

SINCIPITAL ENCEPHALOMENINGOCELES
(after V. Meyer, 1890)

Description:	
(1) *Naso-Frontal*	Site of hernial aperture is between frontal and nasal bones.

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(2) *Naso-Ethmoidal*	Between frontal, nasal, and ethmoidal bones. Tumour situated on anterior edge of nasal bone.
(3) *Naso-Orbital*	Between frontal, ethmoid and cervical bones. Tumour situated in medial curve of eye on anterior part of orbital cavity.

BASAL ENCEPHALOMENINGOCELES

(after Heinreke and Safranek, 1926)

(4) *Spheno-Pharyngeal*	Through the sphenoid bone, or between it and the ethmoid, coming down into nasopharynx.
(5) *Intra-Nasal*	Through the lamina cribrosa appearing as an intra-nasal tumour.
(6) *Spheno-Orbital*	Through the superior orbital fissure, entering the orbit behind the eyeball.
(7) *Spheno-Maxillary*	Through superior orbital fissure and continuing downwards through the infra-orbital fissure into the sphenomaxillary fossa. Tumour appears medial to the remains of the mandible or in zygomatic regions.

OTHER SITUATIONS

Aural	Jaenech, Shreyer and Sprenger, 1926–1941.
Temporal Region	

He gave an account of 34 cases of encephalomeningoceles previously reported in literature and added one of his own. He also reported that the first case had been discovered by Richter in 1813.

A typical encephalomeningocele is recognizable by various criteria:

(1) A pulsation synchronous with the cerebral pulsation;
(2) An impulse on coughing;
(3) Cerebral effects of compression of the tumour which are, vomiting, slowing of the pulse and even unconsciousness.
(4) Transparency;
(5) Radiological evidence of a skull defect.

Many of the tumours, however, are solid, or only partly cystic and do not exhibit any of the characteristics I have just mentioned and it is also extremely difficult to demonstrate radiologically small deficiencies in the skull bones.

The basal forms are, however, liable to be mistaken for benign nasal polypi and, if appearing in the nasopharynx, even for adenoidal vegetation, though the presence of a cleft palate would suggest deficiency in the basis cranii.

Exner wrote of six such cases which were brought about, he considered, by faulty closure of the hypophyseal duct.

Till comparatively recently the view generally accepted, which was propounded by Schmidt in 1900, was that all these tumours were varieties of encephalomeningoceles, cut off in early fœtal life by abnormal development

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of the cranial bones. It was thought that the original connection with the primitive anterior cerebral vesicle had been obliterated either wholly or in part.

More recently a number of Pathologists have taken a different view. Bretton and Robinson in 1946 recorded two cases. In one, the tumour showed primitive tissue of the nature of medullary epithelium and not only was astrocytomatous neuroglial tissue present but also evidence of differentiation into ependyma retina and choroid plexus. Berblinger reported a case some 20 years earlier and was of the opinion that in early fœtal life a portion of nervous tissue had been separated which had limited powers of differentiation, that is to say an area of neuro-ectoderm had failed to become invaginated during the closure of the neural tube. The tumour would thus more accurately be termed a blastoma or hamartoma, that is to say a developmental displacement of tissue.

Morley and Cross in 1957, in their case, clearly identified glial tissue throughout the length of the stalk of a solid tumour presenting at the inner canthus of the eye of a baby. It was considered that this fact supported Berblinger's view in that the tissue was glial throughout and no other nerve cells were present.

It would, therefore, seem that some of the cases recorded, the tumour was an encephalomeningocele more especially when it herniated into the orbit where undoubtedly teratomata, that is to say tumours derived from more than one germinal layer, had been encountered.

The group with which we are particularly concerned this afternoon may more accurately be described as hamartomata. The term glial ectopia which Robinson suggests, is I think preferable to nasal glioma for there is no suggestion of malignant transformation. The treatment is more controversial. Biopsy is tempting but can be inconclusive and even dangerous for it is possible to open up the cerebrospinal pathway with consequent meningitis. Rhinologists have tended to remove the tumours by lateral rhinotomy but some Neuro-Surgeons prefer craniotomy and urge that it is always wiser to inspect adequately the cribriform plate, feeling that the complete severance of any connection between meningocele and cranial contents is imperative even if the tumour should subsequently be found to be a glial ectopia. Robinson particularly has stressed that the distinction between the two forms of tumour can only be made on very accurate histological sectioning.

I am much indebted to Mr. W. A. Mill, St. Thomas's Hospital, and to Mr. Charles Smith of York for kindly making available the case notes from St. Thomas's Hospital.

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CHARLES SMITH, F.R.C.S., D.L.O. said: In the considerable literature under the heading of anterior encephalocœles, nasal gliomata and ectopic brain tissue etc., some 50 or more lesions of the type that we have been considering are described. On more than one occasion biopsy or attempted removal has been complicated by meningitis, and in some cases death. I feel that despite the happy outcome in all of Mr. Lister's cases and the eventual success of the operation on the case described by Mr. Seymour Jones, a nasal polyp in a baby, with or without swelling on the same side of the bridge of the nose, needs to be treated with great caution. Serious consideration should always be given to exposure of the anterior cranial fossa, and repair of any defect in the cribriform plate when an attempt is made to remove the tumour.

K. G. MALCOMSON, M.D., F.R.C.S, F.R.C.S.E. said: I would like to congratulate Mr. Lister on his presentation of this rare and interesting condition. I have encountered it once, in a child of 5 months of age. Her mother, a nurse, observed a complete unilateral otherwise symptomless nasal obstruction soon after birth. Advice was sought when a swelling in the nostril and homolateral epiphora developed with a head cold. On examination a pale non-pulsatile swelling was found attached to the nasal vault, easily compressible without reciprocal fontanelle bulging (and vice versa), and non-expansile on jugular pressure. A meningo-encephalocele could not be excluded. At 12 months of age neurosurgical investigation was proceeded to: intrathecal indigo-carmine suffused the nasal tumour and the diagnosis of meningo-encephalocele was strengthened. Nasal removal was considered too dangerous. Craniotomy revealed a tongue of yellowish cerebral tissue 5·0 cms. in diameter extending from the inferomedial surface of the frontal lobe to a dural and bony defect immediately anterior to the olfactory bulb and cribriform plate, and leading into the nasal vault. The process was divided and the dural defect sealed with muscle graft and fascia.

Six weeks later the nasal tumour was removed by dividing its attachments in the nasal vault: histology—nasal glioma.

The misleading clue in the investigation was tinting of the glioma by indigo-carmine. I would like to hear Mr. Lister's suggestions about establishing the diagnosis between a meningo-encephalocele and a glioma when the clinical features are equivocal, for operative treatment of the former may be hazardous whereas nasal gliomectomy is comparatively simple and safe.

Discussion on Amyloidosis of the Larynx

A. P. FULLER said: I wish to present this patient of Mr. Hogg's as a case of presumed localized primary amyloidosis of the larynx.

She is a housewife, now aged 54. She was first seen in *April, 1950*, complaining of hoarseness. Since she was a girl she had always been husky, but following an accident in 1946 (she was knocked off her bicycle) her voice had been worse. Indirect laryngoscopy showed a polypoidal swelling on the anterior half of both vocal cords. Later that year she was admitted for direct laryngoscopy and biopsy of the polypi. Histological examination of the small fragments removed showed a normal epithelium with minimal inflammatory changes.

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She was next seen in *January, 1961*, because her voice which had remained hoarse had got worse in the preceding few months with in addition occasional attacks of inspiratory stridor. Examination this time showed a very large swelling of the right vocal cord. Direct laryngoscopy showed multiple greyish sessile polypi on the upper surface of both vocal cords. The polypi on the left side were stripped off the vocal cord. Those on the right side were untouched to prevent post-operative web formation. Histological examination of the polypi corresponded with that of primary amyloid.

After operation she was given a course of Dexamethasone 0·5 mgm. b.i.d. starting in *March, 1961*, but although first impressions were that the amyloid mass on the right side was getting smaller this was not confirmed. At the end of 3 months there was no real change so the corticosteroid was gradually discontinued.

In *August, 1961*, she was admitted for removal at direct laryngoscopy of the amyloid on the right side. The left side had remained free from amyloid. At this laryngoscopy all the remaining amyloid tissue was removed piecemeal. Following this she became aphonic but this was considered to be functional. She rapidly responded to speech therapy. As she had been given cortisone she was given cortisone cover for the third laryngoscopy. She is now not taking any.

Investigations were performed to exclude any chronic sepsis as a cause of her amyloidosis. All were negative apart from a raised blood sedimentation rate (33 mm. in *November, 1961* and 40 mm. in *February, 1962*). It is difficult to interpret the significance of this as serum protein and flocculation tests have been normal and the paper electrophoresis showed a normal pattern. These tests were performed at the same time as the blood sedimentation rates. This may be part of the disease and Symmers (1956) points out that the sedimentation rate is usually considerably raised in primary amyloidosis. A Congo red test was performed 3 months after the last operation and it gave a negative result. It is interesting to note that no colour change was seen in the larynx indicating that the removal of the amyloid tissue had been complete.

The paraffin blocks from the first laryngeal biopsy which Dr. Pugh (St. Albans City Hospital) has kindly made available have been re-sectioned and examined by Dr. J. McAlpine (Institute of Laryngology). The hæmatoxylin-eosin stained sections showed small fragments covered by squamous epithelium. The subepithelial connective tissue was replaced by broad sheets and small irregular areas of a homogenous acellular substance whose staining reactions were characteristic of amyloid.

In the light of these findings this case must be considered as a recurrence of laryngeal amyloidosis with a 10-year interval.

Simple removal of the amyloid "tumour" by the most practicable route would appear to be the most successful treatment. Small collections can be removed easily at direct laryngoscopy. If necessary a laryngofissure should be undertaken to allow better access.

Following the lead of McCall and Fisher (1953) this patient was given cortisone systemically, though interstitial cortisone was not given. Animal experiments have shown that steroids can accelerate the production of experimental amyloidosis. Peräsalo and Latvalahti (1954) showed that adrenocortical extract and cortisone increased the development of amyloid in mice receiving injections

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of sodium caseinate. However, objection may be raised on the grounds that there is no direct relationship between the experimental animal and human amyloidosis. But West and Newns have described in 1952, a patient, aged 29, with rheumatoid arthritis present for 3 years , who after treatment for 3 months with cortisone acetate, developed jaundice and hepatic enlargement. Nine months later after continuing with cortisone he died from systemic amyloidosis. Throughout treatment he received calcium caseinate ("Casilan") daily. At autopsy his liver weighed 6,470 gms. and about 95 per cent. of it was amyloid. Their case would seem to provide a connecting link between human and experimental amyloidosis. In amyloid disease cortisone should not be given; especially in association with a high protein diet.

I would like to thank Dr. McAlpine for his valuable assistance with the pathology and Mr. Hogg for his advice and permission to present his case.

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Discussion on Amyloid Tumours

Mr. R. D. Stride, F.R.C.S.E. said: That to establish a firm diagnosis of primary amyloid tumour might present considerable difficulty and that in any case the diagnosis should only be provisional.

He reported the case of a single woman aged 52 years, who was first seen $3\frac{1}{2}$ years previously complaining of a swelling over the root of the nose that had been present for 9 months. It presented as a slowly growing irregular, firm but painless swelling at the glabella and appeared to have eroded the anterior wall of the frontal sinus: destruction of both anterior and posterior walls of the sinus and intersinus septum was confirmed radiologically. Surgical exploration revealed a vascular tumour with extensive local bone erosion. Bence Jones protein and Wasserman reaction were negative as were X-rays of the remainder of the skeleton. Serum albumen 4·0 per cent., Globulin 2·9 per cent. Pathological opinion varied between primary amyloid tumour and plasmacytoma.

Further surgery was performed with extensive resection of bone. Professor Victor Lambert and Mr. R. T. Johnson at this time both considered the tumour to be malignant while the pathological report noted the presence of amyloid change in a malignant process. When reviewed recently she was symptomless and there was no evidence of recurrence.

One point of interest in this case lies in the difficulty in settling the diagnosis: primary amyloidosis? Solitary myelomatosis? Amyloid change in a malignant process? It is hoped that a long term follow up will finally elucidate this problem. Perhaps the application of the new microscopic and biochemical techniques as described today by Professor Friedmann may later assist in establishing a firm diagnosis.

Another point of interest lies in the unusual situation of the tumour. Although nasal amyloid is uncommon, primary amyloid of the frontal sinus appears from literature to be very uncommon.

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