The prime factor in this method is the use of nitrous oxide with a percentage of oxygen at or near that of atmospheric air, thereby ensuring a lack of hypoxia.

The advantages claimed for the method are its added safety, the smoothness of the operating conditions, and its suitability for even quite young children.

My thanks are due to the dental surgeons and lady attendants at these clinics for their invaluable help, and to Dr. G. F. Bramley, County M.O.H. for Gloucestershire, for his interest in my notes.

REFERENCE

Klock, J. H. (1955). *Curr. Res. Anesth.*, 34, 379.

Medical Memoranda

Bell's Palsy

The precipitating factor in isolated peripheral facial nerve paralysis (Bell's palsy) is generally stated to be a circumscribed lesion of the nerve at the stylomastoid foramen. This lesion is thought to result in a swelling of the trunk with an upward extension into the facial canal. Conduction in the nerve is blocked either by compression against the surrounding bone or by interference with its blood supply.

The following animal experiments are of some interest with regard to the possible mode of production of this type of injury. In the course of a study of the central connexions of the facial nerve in the pig, a short series of degenerative experiments were carried out, as follows. The cervical branch of the nerve was cut under anaesthesia in three pigs at the point where it lies just medial to the angle of the mandible. After a variable interval the nervous system was fixed by means of bilateral perfusion with 5% formol saline *in vivo*. The facial nerve and its cervical branch were removed on both sides and examined by means of serial sections stained with osmic acid. The intrapontine segment was studied by means of the Bielchowsky silver pyridine technique.

Histologically, the uninjured facial nerve was normal throughout in each animal. On the side of the operation Wallerian degeneration was seen to be complete in the cervical branch distal to the site of section. The remaining findings on this side are shown in the Table.

Experimental Findings other than Wallerian Degeneration

	Pig 1	Pig 2	Pig 3
Days after operation sacrificed ..	9	12	22
Cervical branch proximal to section:			
Swelling of fibres	++	++	++
Interfascicular fibrosis ..	++	+	+
Facial trunk*:			
Extracranial:			
Swelling of fibres	+	+	+
Interfascicular fibrosis ..	+	+	+
Facial canal:			
Swelling of fibres	+	+	+
Interfascicular fibrosis ..	+	+	++
Capillary proliferation ..	+	++	++
Disintegration			++

* No abnormality between internal auditory meatus and facial nucleus.

Retrograde swelling of nerve fibres is the result we expect from any nerve injury, and was obvious under the microscope at all levels from the site of operation to the internal auditory meatus. The infiltration of fibrous tissue between the fasciculi of the trunk and of the cervical branch was a surprising finding in the absence of Wallerian degeneration. The absence of any round-cell infiltration in routine stains of the same tissues ruled out an inflammatory process as the cause of this reaction. There was an abundance of freshly formed capillaries in the epineurium of the facial trunk.

The feature of special interest is the condition of the intracanalicular facial nerve in the third animal. Two-thirds at least of the fibres were shrunken or misshapen. Although the core of the trunk showed some ensheathed and com-

paratively normal nerve bundles, peripherally there was a partial or complete absence of perineurium, masses of injured nerve fibres lying free in the connective tissue stroma.

In isolated human facial paralysis, material for histological examination is necessarily scant. Cases which have come to operation have not infrequently shown a visible swelling of the trunk at, and just above, the stylomastoid foramen. The very few histological examinations that have been made have shown no evidence of inflammation (Cawthorne, 1951). The rapid recovery of 80% of cases indicates that Wallerian degeneration is exceptional.

The present findings give some grounds for speculation with regard to the immediate cause of the nerve block in Bell's palsy. The integrity of the central fibres of the intracanalicular trunk in the third animal with damage to the peripheral ones is strongly suggestive of a compression injury: the reverse would be expected to occur with an ischaemic lesion. The cause of the swelling is, of course, unexplained. It is noteworthy that a lesion sufficient to give rise to considerable damage to the intracanalicular facial nerve in the pig may be situated well beyond the termination of the facial trunk. The same possibility should perhaps be borne in mind whenever the aetiology of Bell's palsy is under consideration.

This work was assisted by a grant to one of us (M. E. L.) by the Medical Research Council of Ireland.

M. J. T. FITZGERALD, M.B.

MARY E. LAW, M.Sc.

Department of Anatomy,
University College, Cork.

REFERENCE

Cawthorne, T. (1951). *Proc. roy. Soc. Med.*, 44, 565.

Agranulocytosis and Severe Leucopenia after Chlorpromazine Hydrochloride

A case of agranulocytosis in a man and of severe leucopenia in a woman following treatment with chlorpromazine are reported.

CASE 1

A man aged 59 with an anxiety state was treated from October 10, 1955, with 25 mg. of chlorpromazine three times daily for one week, 50 mg. three times daily for a second week, and then 100 mg. three times daily until November 29. Over 12 g. of chlorpromazine hydrochloride was given during eight weeks, the only additional treatment being sodium barbitone, 10 g. (0.65 g.), at night. On November 29 the patient became very ill with severe pharyngitis and treatment with chlorpromazine was stopped.

On admission to hospital he was severely ill with membranous pharyngitis, temperature 102° F. (38.9° C.), but no other significant abnormal physical signs. The haemoglobin was 77%, white blood count 800 (100% lymphocytes, no polymorphonuclears present in peripheral film). The sternal marrow showed normoblastic erythropoiesis; megakaryocytes in normal numbers; almost complete absence of granulopoiesis; 9% myeloblasts, 1% promyelocytes, no further neutrophil maturation; no abnormal cells; no evidence of leukaemia.

The patient was treated with cortisone and antibiotics and was afebrile and greatly improved, with a normal pharynx, in three days. The neutrophil count increased slowly; one week later the peripheral blood film showed 56 polymorphs per c.mm., and sternal marrow showed evidence of recovery, myelocytes being seen. The total neutrophil count continued to rise to 10,080 per c.mm. on December 16 (after 20 days). The patient recovered normal good health.

CASE 2

A woman aged 61 had been a mental hospital patient since 1941, when she was aged 47, with a diagnosis of high-grade mental deficiency and paranoid psychosis. During a transient infection in 1942 the white cells numbered 9,000 (polymorphs 78%, lymphocytes 18%). On admission and subsequently she was in good physical health. On account

of increasing tenseness and excitement she was treated from May 16, 1955, with 25 mg. of chlorpromazine hydrochloride three times daily, increased to 100 mg. three times daily until September 21, when the dose was reduced to 50 mg. three times daily.

On November 5 she looked ill and her temperature was 99.8° F. (37.7° C.). No abnormal physical signs were found. Chlorpromazine was stopped, a total dose of 41.4 g. having been given in 171 days. On November 7 she was flushed, her voice was hoarse, and she said she had a "cold." A few basal crepitations were heard in the chest. The haemoglobin was 70%, and the white blood count 1,500 (polymorphs 32%, lymphocytes 57%, monocytes 11%). Penicillin, 500,000 units twice daily, was given. Two days later she was flushed and excited, her throat was reddened, and crepitations were heard at the bases. Her temperature was 99.2° F. (37.3° C.) and pulse 72. White cells numbered 1,200 (polymorphs 34%, lymphocytes 60%, monocytes 6%). On November 11 sternal marrow puncture suggested some deficiency of the white cell series, with shift to left indicating regeneration of granulocytes.

On treatment with penicillin the patient's fever settled over the next five days. The white cells rose to 3,500 (polymorphs 63%) on November 18, and to 4,500 (polymorphs 63%, lymphocytes 32%, monocytes 5%) on December 29. The patient has regained normal physical health.

COMMENT

Agranulocytosis following treatment with chlorpromazine has been reported by Munch-Petersen (1954), Lomas (1954), Tasker (1955), Boleman (1955), Prokopowycz (1955), and Shapiro (1955). Giacobini and Lassenius (1954) reported one case among 147 patients treated, Goldman (1955) four cases in the treatment of about 1,000 patients, Barsa and Kline (1955) two cases during the treatment of 300 patients. Lomas, Boardman, and Markowe (1955) refer to seven further unpublished cases of agranulocytosis following treatment with chlorpromazine.

In the course of treatment with chlorpromazine the white blood count usually shows little change, though occasionally a slight neutropenia is found in the early weeks of treatment. Andersen (1954) reported two cases with severe but symptomless leucopenia, the blood counts returning quickly to normal when treatment was stopped.

Our first patient became dangerously ill with agranulocytosis lasting some days, but recovered after treatment. The cases previously reported have mostly been in women: a high proportion were fatal. Our second patient became ill with severe leucopenia, and there was no evidence of the "normal" response to infection which Anton-Stephens (1954) found in patients with intercurrent infection on chlorpromazine treatment. The severe leucopenia in this case might have resulted in a more serious illness had the drug been continued and no antibiotic treatment given.

These further cases suggest that the serious, and often fatal, toxic effects of chlorpromazine on the bone marrow may be more frequent than published reports have hitherto suggested. This possibly fatal complication of treatment with chlorpromazine should be recognized by those who prescribe this drug.

J. C. L. ADAMS, M.D., M.R.C.P.,

K. D. F. CORTI, M.B., B.S.,

Q. J. G. HOBSON, D.M., M.R.C.P.,
West Middlesex Hospital, Isleworth.

REFERENCES

- Andersen, H. (1954). *Ugeskr. Læg.*, **116**, 1733.
Anton-Stephens, D. (1954). *J. ment. Sci.*, **100**, 543.
Barsa, J. A., and Kline, N. S. (1955). *A.M.A. Arch. Neurol. Psychiat.*, **74**, 280.
Boleman, A. P. (1955). *J. Amer. med. Ass.*, **157**, 364.
Giacobini, E., and Lassenius, B. (1954). *Nord. Med.*, **52**, 1693.
Goldman, D. (1955). *A.M.A. Arch. intern. Med.*, **96**, 496.
Lomas, J. (1954). *British Medical Journal*, **2**, 358.
— Boardman, R. H., and Markowe, M. (1955). *Lancet*, **1**, 1144.
Munch-Petersen, S. (1954). *Ugeskr. Læg.*, **116**, 1787.
Prokopowycz, V. (1955). *J. Amer. med. Ass.*, **157**, 1042.
Shapiro, N. (1955). *S. Afr. med. J.*, **29**, 673.
Tasker, J. R. (1955). *British Medical Journal*, **1**, 950.

Acute Hallucinatory Episode following Hexamethonium Bromide

A married woman aged 49 was admitted to the Ormskirk County Hospital on October 15, 1954, with a complaint of occipital headache and dizziness for the past two years, together with a dull ache in the loins for the last two months. The latter was improving at the time of admission. She also complained of swelling of her face each morning for the last two months, which passed off during the day. There was no previous or family history of mental disorder. The patient's mother had died aged 47 following a "stroke," the father of coronary thrombosis at the age of 75, and an only brother suffered from "blood pressure."

Examination showed her to be a pallid woman of medium height and build. The blood pressure was 260/160, and there was moderate papilloedema and some retinitis, more obvious in the left eye. The C.N.S. and other systems showed no abnormality. Total serum protein, 5.9 g.; albumin, 4.5 g.; globulin, 1.4 g.; A./G. ratio, 3.2:1. Total and differential blood count and film showed nothing abnormal. There were no casts or red blood cells in repeated urine specimens, but a fair number of pus cells were present. Albumin varied from 100 to 30 mg. per 100 ml. The blood urea varied between 45 and 55 mg. per 100 ml. A diagnosis of essential hypertension passing to malignant hypertension was made.

A trial dose of hexamethonium bromide was given on October 26—that is, 25 mg. intramuscularly—and 15 minutes later the blood pressure was 160/120. Thirty minutes later it was 190/140. The former reading was the lowest throughout the treatment. She was then placed on 50 mg. intramuscularly six-hourly and received this dosage until the morning of October 31. During this time she received 575 mg. of hexamethonium bromide, but she complained on October 27 that she had felt a loss of power in her right arm for 15 minutes. Clinical examination did not disclose any sign of a cerebral vascular lesion or other abnormality, and the treatment was continued.

On the morning of October 31 she complained that a man was going to shoot her and explained that it was rather unfair because her headaches were better. She was not distressed about this belief. The hexamethonium bromide was stopped, but in the evening she walked out of the ward in her nightdress, and when brought back informed the house-physician that she had walked out to avoid being shot. The same evening she was transferred to the mental observation ward. The next morning she stated that she had seen four cannons mounted on the walls of the medical ward, that a man had come round the ward with a gas tube and had first gassed and then cut the throats of other patients. She believed that she had spent the night in an "electric bed" because of the weird sensations in her body and that she had heard the night nurse say that she was immoral and a prostitute and also suffering from venereal disease. She became distressed on describing this, but quickly recovered. She was also convinced that somebody wanted to "get rid" of her, but could not name the person or persons concerned. There was no clouding of consciousness and restlessness, and orientation was normal. Her behaviour as regards meals, ward discipline, etc., was quite normal, and there was no sign of confusion in her speech or attitude, such as would be expected with a cerebral lesion or bromide intoxication.

She remained in this state for three days, but by November 5, although quite willing to discuss her hallucinations, she had gained partial insight into them and was shy and shamefaced when they were touched upon. The next day she was fully recovered and said, "I must have been daft, but it did seem real."

I wish to thank Dr. J. Erskine Howie, Dr. G. Sanderson, and Dr. Thelwall Jones for advice in the preparation of this report.

T. P. SMITH, M.R.C.S., D.P.M.,
Assistant Psychiatrist, Ormskirk County Hospital.