Supplementation of an anaesthetic usually infers the addition of further volatile or intravenous agents. As hyperventilation will have a negligible effect on nitrous oxide uptake, Dr. Leaming is merely potentiating or enhancing nitrous oxide anaesthesia by simultaneously reducing cerebral flow.—We are, etc.,

J. M. LEIGH.
C. M. CONWAY.

Department of Anaesthetics,
Westminster Hospital,
London S.W.1.

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SIR,—I have read Dr. H. L. Leaming's letter (4 October, p. 51) on awareness during anaesthesia, and would be the first to congratulate him on a very fine clinical record.

However, his remark that "there is no justification or rational reason for administering a greater concentration of oxygen in the respired gases than that existing in the atmosphere" must surely be in doubt. Recent studies have demonstrated the existence of an intra-pulmonary arteriovenous shunt of some 10% during the state of general anaesthesia, and the effect of this added to the effect of ventilation/perfusion inequalities is to lower the arterial oxygen tension—a potentially dangerous situation. It is to overcome this fall in oxygen tension that has prompted anaesthetists to increase the oxygen concentration in the inspired gas mixture, and it is surely the difficulty in combining this with the problems of maintaining unconsciousness in the patient that has stimulated the recent letters on the subject in your columns.—I am, etc.,

Military Hospital,
Colchester, Essex.

G. W. MORRIS.

sity of Edinburgh, for carrying out the pyocine typing of the strains studied, and to Miss Dora A. McNellis for technical assistance.

—We are, etc.,

W. A. BLACK.

R. W. A. GIRDWOOD.

University Department of Bacteriology,
Royal Infirmary,
Glasgow C.4.

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Tennis Leg

SIR,—In your leading article (6 September, p. 543) no mention is made of soft-tissue radiography as an aid to the diagnosis of tennis leg. Occasionally a gap in the gastrocnemius at its insertion into the Achilles tendon is visible in lateral views of the leg.

The Figure shows a radiograph of the right leg of a 56-year-old woman who had pain in the calf of sudden onset. Examination revealed local tenderness and reduced power in the calf, but no palpable gap, bruising, or oedema.—I am, etc.,

DOUGLAS GOLDING.

Princess Alexandra Hospital and
Harlow Group,
Herts and Essex.

Carbenicillin Resistance in *Pseudomonas aeruginosa*

SIR,—We were interested to observe the findings of Dr. J. H. Darrell and colleagues (19 July, p. 141), as we have been investigating recently the emergence of strains of *Ps. aeruginosa* which show degrees of resistance to carbenicillin higher than those described by them and in previous reports.¹ The detailed findings are presented in the Table, from which it can be seen that six of the ten strains isolated showed, when tested against carbenicillin, a minimum inhibitory concentration (M.I.C.) of 5,000 µg./ml. or more. Initially the M.I.C.s were measured by tube-dilution and replica plate methods, but the results here presented were obtained after retesting using the method of Dr. Darrell and colleagues.

All patients, with the exception of Case 8, who had received a 10-day course of carbenicillin, had received ampicillin on admission and prior to the isolation of the carbenicillin-resistant strains of *Ps. aeruginosa*. It is felt that the presence of these resistant strains bore no relationship to previous exposure to antibiotics, in particular ampicillin, as it can be seen from the Table that there was considerable variation in the interval between

institution of the antibiotic therapy and the isolation of *Ps. aeruginosa*. In two instances—namely, Cases 2 and 6—highly resistant strains were isolated after only four days of hospitalization and ampicillin therapy, whereas with Case 1 the resistant *pseudomonas* was first detected 30 days after antibiotic therapy had been terminated.

In no instance was the *Ps. aeruginosa* considered to be significant on clinical grounds, which would substantiate the opinion expressed recently that the mere presence of this organism is no absolute indication for specific antibiotic therapy.² This clinical impression was reinforced by failure in most instances to reisolate the same organism from repeat specimens. The presence of several pyocine types and the absence of a definite epidemiological pattern would suggest that cross-infection played no significant part in the spread of these organisms.

Since the completion of the series we are now isolating carbenicillin-resistant strains of *Ps. aeruginosa* with increasing frequency in this laboratory.

We wish to express our thanks to Dr. R. R. Gillies, of the bacteriology department, Univer-

Patient	Type of Specimen	Number of Days between Admission and Isolation of Resistant <i>Pseudomonas aeruginosa</i>	M.I.C. (µg/ml.)	Pyocine Type
1	Burn swab	60	5,000	1c†
2	Burn swab	4	10,000–20,000	1c
	Burn swab	12	< 35	1c†
3	Burn swab	8	10,000	1b
4	Urine	30	150	1b*
5	Urine	30	300	1b*
6	Burn swab	4	10,000	1a
7	Burn swab	4	< 35	1h
	Burn swab	10	10,000	1a
8	Burn swab	14	10,000–20,000	1a

* These strains are absolutely identical and differ very slightly from the other 1b subtype.

† These strains are absolutely identical and differ very slightly from the other 1c subtype.

Fibrin Degradation Products

SIR,—We have noted the report of Dr. J. Bonner and others (19 July, p. 137) on the levels of fibrin degradation products (F.D.P.) in the serum of healthy women during normal pregnancy, labour, and the puerperium.

We have made a similar study,^{1,2} but with somewhat different findings. We do not agree that the level of F.D.P. is normal in late pregnancy, since we find levels approximately twice normal in sera of women 35 or more weeks pregnant. This confirms the observation of Woodfield *et al.*³ However, we do agree that a further rise occurs during labour. Our observations indicate that this is maxi-

mal in the first four hours after delivery of the infant; the level declines thereafter and at 24 hours is the same as or a little higher than that seen in late pregnancy and at the onset of labour. The level of F.D.P. is even higher in 50% of women with twin births. We have not made any observations later than 24 hours after delivery.

Recent findings⁴ regarding the haemagglutination inhibition assay have shown that the assay can be considerably simplified by the substitution of human for sheep red cells. A uniform level of protein for dilution of samples and standards should be used throughout the assay to achieve reliable results. We have largely abandoned the use of the microtitre (or similar) system, since we found that it introduces a consistent error, as it tends to produce less than doubling dilutions, resulting in fallaciously low readings. In addition, the currently used assay which involves red cell agglutination (rather than a settling pattern of cells) is easier to read in a plate with larger wells. We have been able to adapt the method to the AutoAnalyzer with similar and even more reproducible results, allowing more certain detection of small differences between samples. Rechecking our previous results on the AutoAnalyzer has confirmed the results mentioned above.—We are, etc.,

C. MERSKEY.
G. J. KLEINER.
W. MARKUS.

Albert Einstein College of Medicine,
Bronx, New York 10461, U.S.A.

A. J. JOHNSON.
New York University Medical Center,
New York, N.Y. 10016, U.S.A.

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Pituitary Dwarfism and Size of Gonads

SIR,—In clinical descriptions of pituitary dwarfism little attention is given to the size of the genitalia.¹ The only reference to small genitalia is made by Brasel *et al.*, who, in their review of 75 patients with pituitary insufficiency beginning in childhood note that in some of the male subjects the external genitalia were small for their age.² No specific mention is made of the gonads.

The possibility that pituitary growth hormone (H.G.H.) plays a role in the growth of the gonads was tested by carrying out measurements of the latter in patients with H.G.H. deficiency. Since this is impossible in girls, only boys were included in the study. The study included 22 children belonging to four groups of pituitary dwarfism: (a) hereditary isolated H.G.H. deficiency; (b) sporadic isolated H.G.H. deficiency; (c) biologically inactive IR-H.G.H.³; and (d) idiopathic pituitary insufficiency including H.G.H. The testicular volumes, estimated by calliper and by orchidometer,^{4,5} of these children is presented in the Figure. It is evident that, with

the exception of two subjects which had previously been given some treatment, in all the

● Isolated HGH deficiency, hereditary. ▲ Isolated HGH deficiency, sporadic. × Biologically inactive IR-HGH, hereditary. ○ Idiopathic pituitary insufficiency including H.G.H.

subjects the testes were small as compared to norms for our population, even before puberty. It is noteworthy that the testicular underdevelopment is most prominent in those individuals with an isolated lack or biologically inactive H.G.H. These findings strongly suggest that H.G.H. plays an active role in the growth and development of the gonads, with no relation to puberty.

A complete report, including longitudinal growth of the testes in children with pituitary insufficiency and their penile size, will be published elsewhere.—We are, etc.,

ZVI LARON.
RA'ANANA SAREL.

Pediatric Metabolic and Endocrine
Service, Division of Pediatrics,
Beilinson Hospital,
Tel Aviv University Medical School,
Israel.

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Formaldehyde Sterilization for Dialysers

SIR,—We wish to stress the importance of achieving an adequate concentration of formaldehyde when this agent is used for the sterilization of haemodialysis equipment.

At one time we were extremely concerned by the frequency and severity of pyrexial reactions in patients undergoing regular dialysis treatment at the London Hospital. Blood cultures were repeatedly sterile. Methods of sterilization then in use were thoroughly reviewed. The Kiil dialysers had been sterilized for 24 hours with a solution prepared in the hospital pharmacy and labelled "2% formaldehyde." Samples of fluid from the dialysate compartment of each dialyser were collected for bacterial culture and colony count after 14 hours' dialysis, and the results are shown in the first column of the Table. One patient was dialysed with a Minicoil dialyser sterilized by gamma-irradiation, and experienced no pyrexial reactions. It therefore seemed probable that the reactions were caused by inadequate sterilization of the Kiil dialysers, and formaldehyde sterilization was temporarily abandoned in favour of 3% acetic acid. No

further reactions occurred and sterilization was shown to be satisfactory (columns 2 and 3 of the Table).

At this point it became apparent that, in error, the Kiil dialysers had been sterilized for three months with 2% formalin. Since 100% formalin is a solution of 34–40% of the gas formaldehyde in water, 2% formalin contains only 0.8% formaldehyde, which has dubious bactericidal properties.¹ When 2% formaldehyde was used again for sterilization there was a significant fall, 100-fold or greater, in the dialysate colony counts (column 4 of the Table), and no further pyrexial reactions occurred.

We recommend, therefore, that if formaldehyde is used in the sterilization of Kiil dialysers its concentration should be not less than 2%.—We are, etc.,

M. MURRAY.
J. R. E. DATHAN.
F. J. GOODWIN.

London Hospital,
London E.1.

REFERENCE

- Sykes, G., *Disinfection and Sterilization*, 1965, 2nd ed., p. 345. London, Spon.

Colony Counts (per ml.) of Dialysate Collected from Dialysers after 14 Hours' Dialysis

Patient	Method of Dialysis and Sterilization			
	Kiil Sterilized by 0.8% Formaldehyde	Minicoil Sterilized by Gamma-irradiation	Kiil Sterilized by 3.0% Acetic Acid	Kiil Sterilized by 2% Formaldehyde
I	5×10^8 <i>E. coli</i> 1×10^{10} <i>Pseudomonas pyogenes</i>	No growth	1×10^5 <i>E. coli</i>	2×10^5 <i>E. coli</i> 1×10^6 <i>Pseudomonas pyogenes</i>
II	1×10^{10} <i>E. coli</i> 8×10^{10} <i>Pseudomonas pyogenes</i>	No growth	—	1×10^5 <i>E. coli</i>
III	3×10^9 <i>E. coli</i> 2×10^{10} <i>Pseudomonas pyogenes</i>	No growth	—	2×10^7 <i>E. coli</i> 2×10^7 <i>Acinetobacter</i>
IV	8×10^{11} <i>E. coli</i> 6×10^{11} <i>Pseudomonas pyogenes</i>	—	3×10^4 <i>Staph. spp.</i>	No growth