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### Notice to Members.

As usual the next and the last number for the year of the "Madras Medical Journal" will be sent by V. P. P. to such of the members as have not paid their subscriptions by October. Many of the members seem to prefer their subscriptions to be collected in this manner. But a few others resent a V. P. P. in spite of a previous warning. It is requested of such members that they may be pleased to send their subscriptions forthwith.

Members resident in Madras are requested to pay up their subscriptions as early as possible. They are reminded that the finances of the Association are in a very fluid state and, unless current subscriptions are paid, it will be impossible to meet all outstanding claims on the Association's funds. As we cannot afford to have a wholetime collecting staff, members are requested to send their subscriptions themselves.



The  
**Medical Journal**  
JOURNAL OF THE MADRAS MEDICAL ASSOCIATION  
PUBLISHED QUARTERLY.

JULY 1938.

No. 3.

Editor :

J. C. DAVID, M.B.B.S., PH.D. (EDIN.).



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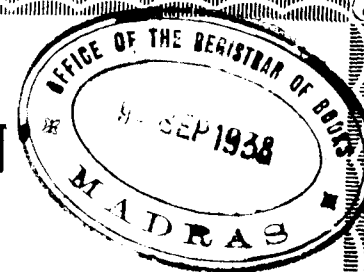
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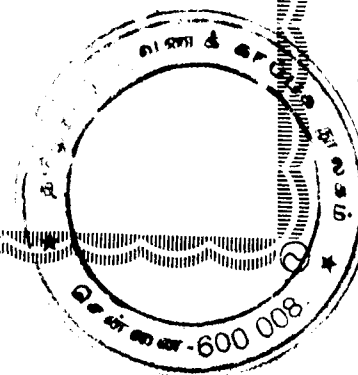
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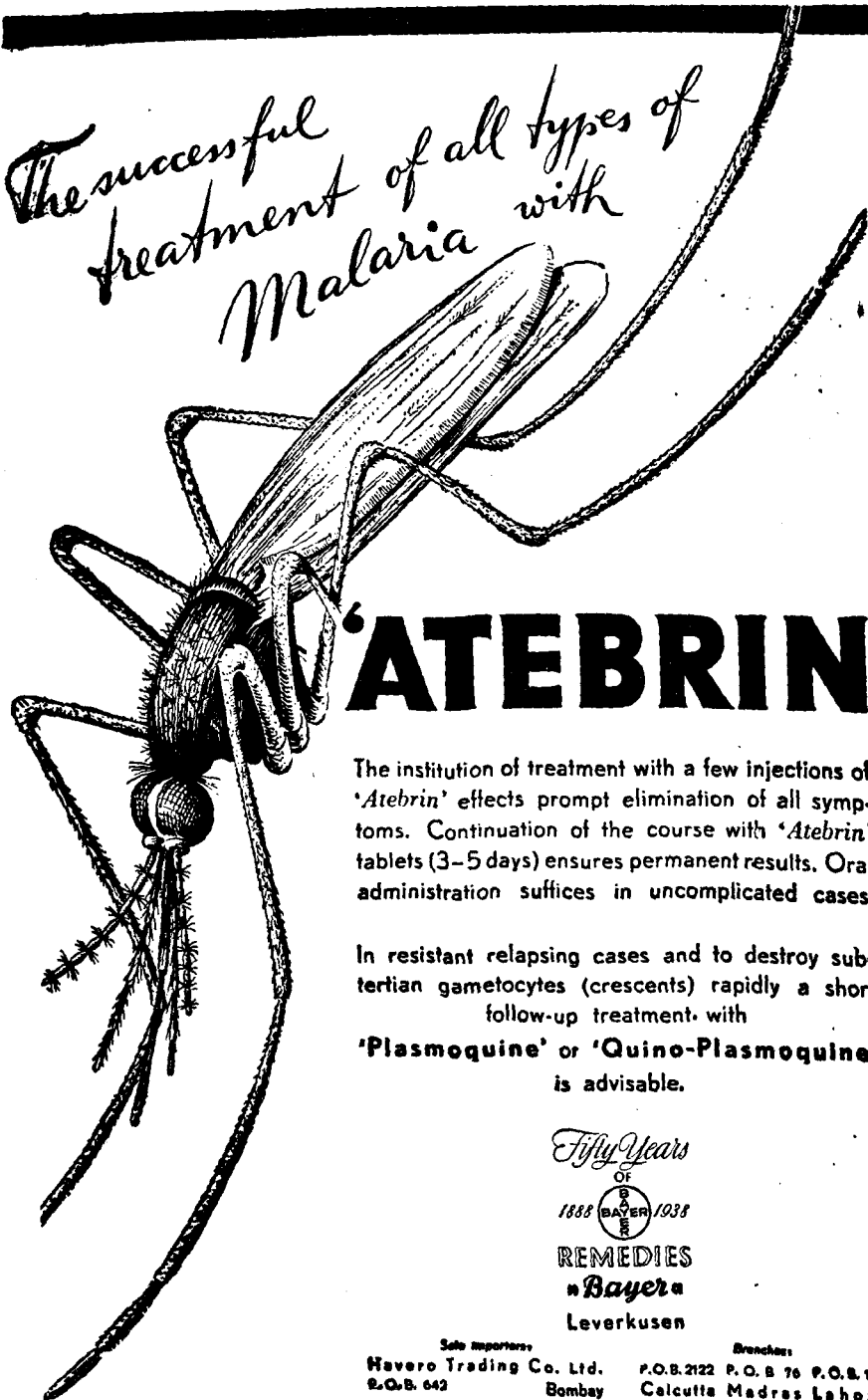
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The  
**Madras Medical Journal.**

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JULY 1938.

No. 3.

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## EDITORIAL NOTICE.

The Madras Medical Journal is issued quarterly, in January, April, July and October about 20th of the month. All Editorial communications, reports, books for review and exchange should ordinarily reach the Editor, The Madras Medical Journal, Dept. of Pharmacology, Medical College, Madras, one month prior to the date of issue of the Journal, preferably earlier. Original articles, clinical lectures, case reports, abstracts, Medical Society addresses are invited. Contributors of original articles will be supplied gratis with twenty reprints of papers, if applications for the same are received by the Editor along with the contributions.

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## THE MADRAS MEDICAL JOURNAL.

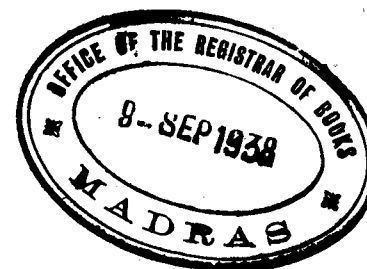
VOL. XVIII.

JULY, 1938.

No. 3.

## CONTENTS.

|                                                                                                              | PAGE    |
|--------------------------------------------------------------------------------------------------------------|---------|
| 1. SPECIAL ARTICLE.                                                                                          |         |
| THE ORIGIN AND EVOLUTION OF THE MADRAS GENERAL HOSPITAL—(Contd).                                             |         |
| By D. V. S. Reddy, M.B., B.S.                                                                                | ... 133 |
| 2. NEUROSYPHILIS—A CLINICAL STUDY.                                                                           |         |
| By P. Kutumbiah, B.A., M.D., M.R.C.P. (Lond.)                                                                | ... 151 |
| 3. AN ANALYTICAL STUDY OF FRACTURES SEEN AND TREATED IN THE ORTHOPÆDIC DEPARTMENT, GENERAL HOSPITAL, MADRAS. |         |
| By N. S. Narasimhan, F.R.C.S. (Eng. & Ire.)                                                                  | ... 161 |
| 4. CLINICAL MEMORANDA.                                                                                       |         |
| (a) CLINICAL CASES FROM THE ORTHOPÆDIC DEPARTMENT, GENERAL HOSPITAL, MADRAS.                                 |         |
| By N. S. Narasimhan, F.R.C.S. (Eng. & Ire.)                                                                  | ... 180 |
| (b) REPORT OF THREE CASES OF ECTOPIC PREGNANCY.                                                              |         |
| By R. C. Krishnan, F.R.C.S.I.                                                                                | ... 186 |
| (c) A CASE OF RETRO-OLIVARY BULBAR SYNDROME.                                                                 |         |
| By M. D. Anantachari, M.B., B.S.                                                                             | ... 190 |
| 5. ABSTRACTS FROM CURRENT MEDICAL LITERATURE                                                                 | ... 182 |
| 6. NEWS AND NOTES                                                                                            | ... 237 |



The  
**Madras Medical Journal.**

The Journal of the Madras Medical Association.

PUBLISHED QUARTERLY.

Vol. XVIII.

JULY 1938.

No. 3.

SPECIAL ARTICLE.

**The Origin and Evolution of the Madras  
General Hospital.**

BY D. V. S. REDDY, M.B.B.S.,

*Vizagapatam.*

*(Continued from the previous issue.)*

**THE STAFF OF THE  
HOSPITAL.**

**Surgeons, their Assistants, etc.**

At a consultation dated 24th May, there is the first reference to Mr. Duncan Munro. He was "Some time ago Surgeon's mate of this place and had behaved himself to satisfaction. He arrived from Malabar coast whither he had gone a voyage." The council ordered that he be entertained as Surgeon of this garrison, "Mr. Robson being lately dead, and we being in want of an able man, there being a great mortality in this place."

(D. & C. 1720, p. 86). On 4th August 1720, Council ordered "The Hon'ble Company having in the 85th Parragh of their letter by the Duke of Cambridge appointed Mr. Munro, Chief Surgeon of this Garrison, on the 1st vacancy in that post and Mr. Robson being lately dead, whereupon the said Mr. Munro was admitted as youngest Surgeon." "Ordered that he do now take place as Chief Surgeon of this Garrison, according to the Hon'ble Company's directions." (D. & C. 1720, p. 130). The other Surgeon at Madras at this time was Andrew Pitchier, who is entered

as arriving on 20th August 1716 Both Munro and Pitchier appear to have continued till 1726. At a consultation dated 22nd June 1725, a petition was read from Munro and Pitchier praying for another assistant in the Hospital. Here is the actual petition. 'Hon'ble Sirs,

The two surgeons' mates were usually maintained in the hospital here by the Hon. Company to assist your petitioners, yet for some months last past, there is not one and the sickly season of the year now approaching, which may require more hands. We entreat your Hon. etc. Council may take it into consideration.

Gentlemen,  
Your most humble servants,  
Andrew Pitchier  
Duncan Munro."

On this petition the following orders were passed:—

"Petition being considered and Mr. Ramsay who is recommended in the general letter from the Hon'ble Masters being willing to act as a mate till a vacancy happens, agreed that he be entertained at 10 Pags. a month to commence the first of next month." (D. & C. 1725, P. 101 & 102). Duncan Muuro resigned in January 1726. George Ramsay was entertained in his place as one of the surgeons of the garrison. (D. & C. 1726, p. 6). An entry in 1728, throws interesting side-light promising an appointment in the Fort St. George for earlier

services at Bencooloon, evidently a very unhealthy place. "The gentlemen of Bencooloon having represented to us that the surgeon we last sent them Mr. Des Champes, is very ill and that the climate disagrees with him so much as to make him resolved to come away should he recover, and Mr. Douglas who has just come from camp being prevailed upon though he dislikes the place very much to return thither in this emergency, when we can get no other person fitly qualified for the same. Agreed that as a consideration for his so doing we do allow him the same dyet allowance as is given to the youngest of the council there and further that if Honourable Masters do not appoint a surgeon out of England *we will call him to the first vacancy that shall happen here after Mr. Barlow.*" In 1729, Dr. Barlow petitioned as follows:—

"Your petitioner was by the Hon'ble Court of Directors sent here in order to succeed as Surgeon on any vacancy which might happen after your petitioners arrival and your petitioner apprehending that there will shortly be a vacancy by the resignation of Mr. Andrew Pitchier.

Your petitioner therefore most humbly begs your Honour etc. that he may succeed the said Mr. Andrew Pitchier." (D. & C. 1729, p. 45).

Andrew Pitchier went away on 14th September 1729 and Nathaniel Barlow was entertained as

surgeon from 25th November 1729. The other surgeon at this time was Mathew Lindsay. In 1726 he petitioned offering his services as Doctor's mate of the Hospital. "Mr. Ramsay of the garrison having been for some time ill and continuing incapable of acting, I beg leave to offer myself to act as mate during his illness with the usual salary and allowances. (D. & C. 1726, p. 71). Within a month, the council read another petition from Mathew Lindsay, surgeon's mate "Mr. Ramsay, one of the surgeons, being deceased, I beg leave to offer myself to succeed him in that station...Mathew Lindsay." The Council ordered "Mr. Lindsay being a universal good character and being judged a man capable in his profession, resolved that he be entertained one of the surgeons of the garrison with the usual salary and allowances." (D. & C. 1726, p. 84-85). This Lindsay died on 24th August 1730 and was succeeded from the same day by Robert Douglas. "President acquaints the Board of the death of Lyndsay, surgeon and proposes Mr. Thriepland to succeed him as one who served at Fort St. David a long time, very capable and diligent ever since he has undertaken that laborious employment and the care of the garrison as numerous as this without any help or encouragement but the Company's pay Dr. Douglas giving in a remonstrance that he would not have gone to the west coast but upon condition of having the first vacancy at this place, which was then promised him as

appears upon the Consultations signed by the late President and Council, assured that Mr. Douglas be allowed to officiate till the Company's pleasure is known, as we can't suppose any agreement so absolute as to exclude the Company's choice." (D. & C. 1730, p. 119).

#### Surgeons' Mates.

A few scattered references occur to the number and the names of Surgeon's Mates in the Hospital of the early part of the 18th century. "Agreed also that Mr. William Douglas who returned on the *Wager* be restored to his former station of Surgeon's Mate of the hospital and that Mr. Robert Turin who has officiated very diligently in that capacity here during the other's absence as well as for some time before, at Fort St. David do continue to act as another Mate at the allowance of 10 Pagodas per month, for that it has always been *usual to have two Mates* here when we could get proper persons, that the present sickly season requires it, and that we may not be in want of a person of that profession to supply any vacancy that may happen at the subordinate settlements." (D. & C. 1738, p. 128).

#### Steward of the Hospital.

"About 1726, there was as steward of the Hospital one Henry Ross. He died intestate and the Council ordered that whatever effects could be found should be taken under the care of the Paymaster. Among the

notes and bonds, there were two, from Duncan Munro for 200 Pags." (D. & C. 1729, p. 98).  
A specimen of application form:

To

The Hon'ble Nathl-Elwick, Esq.,  
President and Governor etc.,  
Council of Fort St. George,

The Petition of Archibald  
Murray.

Humbly Showeth,

That your petitioner having been but a surgeon in which employ he hath behaved himself to satisfaction as will appear by the discharge which Captain Rigby at his request gave your petitioner and being desirous of serving the honourable company which was the inducement that led him to leave ship *Enfield*.

Your petitioner therefore humbly prays to your honour etc. will entertain him as a Surgeon for the west coast where he is informed there is a vacancy and as in duty bound,

Your petitioner shall ever  
pray etc.

(D. & C. 1723, p. 87).

**Privileges, private practice, etc.,  
of surgeons.**

The duties of the Doctors have already been mentioned. By the end of the 1st quarter of the 18th century, the honourable company seems to have allowed to the Surgeons of Fort St. George the

privilege of examining and selecting candidates for the post of a surgeon at subordinate stations. Duncan Munro and Pitchier examined Archibald Elliot, a surgeon who offered his services to go to the west coast and found him to be capable of such employment. The Council thereupon agreed to entertain him. (D. & C. 1722, p. 89). This Elliot desired to be discharged in 1726 and in his place, Robert Douglas offered his services to go to Fort Marlborough. (D. & C. 1726, p. 67 and 69).

It is also interesting to note that the two surgeons of the Fort in 1734, Doctors Barlow and Douglas were among those who were appointed Aldermen for the town of Madras. They did not accept the employment and were therefore fined by the Mayor's Court. They prayed to be released from these employments and applied to the President and Council for relief of fines. Both the requests were granted. (D. & C. 1734, p. 86). One of the surgeons of the hospital Dr. Munro had also the unique honour of being chosen as the Aldermen of Madras, after his retirement in 1727.

The surgeons were not prohibited from accepting presents. Dr. Bulkley was the recipient of an emerald ring worth about 20 pagodas from the Nabob in 1706, when he accompanied an English mission. There are also indications that the Doctors benefited by some wills. Here are a few examples:—

John Turton made a will bequeathing to Dr. Thomas Robson 25 pagodas. (D. & C. 1720, p. 76).

Henry Davy made a will desiring that the Hon'ble Governor would reward Dr. Pitchier for all his care and trouble. (D. & C. 1720, page 78).

Charles Davers made a will leaving to Dr. Pitchier the sum of 30 pagodas "in case I die of my present illness and that I did not pay him before I die". (D. & C. 1720, p. 164).

John Acton of Fort St. George—Will dated 16-8-1721. "I bequeathe to my beloved friend, Dr. Munro, three pagodas for a ring". (D. & C. 1721, p. 113). Surgeons were also allowed private practice but the Honourable Court were pleased to order that the surgeons should find their own medicines, for their own private practice. The surgeons therefore annually indented for a sufficient quantity of such medicines to be put up by their own apothecarys and sent from England. (D. & C. 1742, p. 122).

Some side-lights on the lives of the physicians and surgeons. Some of the surgeons and physicians made a decent fortune. Doctor Edward Bulkley paid into the Right Honourable Company's cash a sum of 1,000 pags. at interest at 8 per cent per annum in 1703. There were others who got deeply into debts. After the death of Dr. Ramsay the question arose whether he made any will. The council ordered Paymaster and Secretary to examine the

papers of the deceased to clear this doubt. None was discovered in the papers. On enquiry, Dr. Pitchier gave them this information. On approach of death, Pitchier put Ramsay in mind of making a will, but Ramsay's answer was what signified a man making a will that was in debt? (D. & C. 1726, p. 89 and 97). Later, a letter from Calcutta discloses that he had also small diamonds of Mr. Maggee of Calcutta. He was also indebted to several people, among whom was one Doctor Thomas Edmonstone who had a bond for £ 138. and John Lauder to whom Ramsay owed 250 pags.

The Doctors seem to have had some private trade. Among the articles that came by the ship 'Goodfellow' and belonging to private persons, was one small packet of gold costing 47 pags. intended for Mr. Munro. (D. & C. 1725, p. 145). In the account of silver delivered by the Company's galleys, there is an entry. "D. M. No. 1. 2,044 ozs. to Mr. Duncan Munro". (D. & C. 1725, p. 163). Occasionally, Doctors got one hind-head of beer from England as did Doctor Douglas. One may note here that in the course of a report on the allowances of wine and arrack to company's servants at Marlborough, it is mentioned that the surgeon was given 30 bottles per month of wine (European liquor) and 9 bottles of arrack. It was also a common practice for the surgeons to purchase wine at the public outcry in Madras. Doctor Lindsay purchased one pipe of Madeira wine for 47 pags.

in August 1730. Dr. Munro purchased Madeira wine one pipe and old wine one pig-head in 1733. Robert Douglas bought Madeira wine, 2 pipes in 1737 and another 2 pipes in 1738 each pipe for sums ranging from 47 pags to 57 pags.

### MEDICINES, ETC.

When the Medicine chests or drugs expected from England did not come or the stores were exhausted before the arrival of fresh supply, the immediate needs were provided in two ways. The Paymaster was either ordered to buy any chest of physic available for sale with private persons or as the private property of Doctors themselves. In 1707, Dr. Bulkley had a chest of physic consigned to him from England and he offered to sell it at 25 per cent advance upon the invoice. As the Company wanted one for Fort St. David, it was purchased and sent thither. Sometimes, a list of medicines urgently required was submitted to the Council requesting permission for local purchase. In April 1711, Dr. Chadsley sends in a list of medicines. "Mr. .... is desired to assist Mr. Chandsley in the procuring what he shall think necessary of them to serve the garrison until the Europe ships may arrive". Occasionally, replacement of medicines was demanded by ships bringing soldiers or going out on expeditions. Thomas Blake, Commander of the ship *Crags*, petitions the President and the Council of Fort St. George in May 1720, representing that 30 soldiers

were suddenly sent on board his ship just before its departure; that as many of the soldiers fell sick on the way during the 9 months, most of the ship's medicines were expended; that he was promised replacement of the medicines spent from the Fort chest of medicines of the Company, intended for the West Coast and when these chests were actually delivered he did not get any recruitment of medicines (page 88). In 1727, a demand for the supply of stores for the Company's ship *Marlborough* was submitted to the Council which sanctioned among other articles "medicine box-one" (page 116). When the Fort St. George establishment was asked to supply medicines to other settlements like Fort St. David and Fort Marlborough and the stores in Madras were not adequate, the Council usually ordered chests or parcels available for sale to be purchased and sent to respective settlements. In 1724, the garrison at Fort Marlborough was in great want of medicines. "We not having sufficient for the supply, it is agreed that the surgeons be permitted to buy a parcel that is now in the place and offered to sale, if they be good" (page 148). These were purchased and an account was produced amounting to pagodas 106-35-40. Again in 1728, the following entry is noted:—

"Mr. Lindsay presents a bill to the Board for 60 pags. for a chest of medicine sent to Fort St. David which were obliged to purchase of him, the Company

not having sent any out for that settlement and those we have had for this place being but barely sufficient for our own use.....ordered that Paymaster do discharge the same" (page 33). It may be noted in passing that a number of private persons, including non-medical men, used to get from England, medicine chests either for their own use or for sale at a profit. George Tempest, shipped on 'Loretto' "one box containing physick" for his own use in 1725. Among the effects of John Blunt of Ingerum who died in 1728 a *physick box* was found in a godown". Once, the supply of medicines failed on account of the loss of ship. in 1722. "The President inform the Board that the Doctors have frequently acquainted him of the want of medicines in the Hospital occasioned by the loss of the *Nightingale*, the annual supplies for the most part being upon her and that there is a parcel in this place, amounting as per invoice £119 sterling, it is therefore agreed that the same be purchased allowing 25 per cent advance and that the amount thereof be paid for, out of cash" (page 142). In 1734, a new procedure is noted when the supply for Fort St. George is insufficient or the full indent sent is not provided. On August 12th of this year, the surgeons sent in a request that the "warehouse-keeper may be directed to deliver them some of the medicines sent out for Fort St. David, there being none of the same in the supply sent for this garrison".

Hon. Sir,

The medicines this year received from the Hon'ble Company, being in several particulars different from the indent sent home, we are greatly in want of several sorts and finding in the Fort St. David invoice of medicines, they have a large supply of some of them, we are obliged to request your honour etc., will direct the warehouse-keeper to deliver us the following particulars out of the said medicines:—

Fol Senæ lb. ii.

Armen. lb. ii.

Camphor oz. . . .

Rad: Valerian Selves oz. vi.

Phials in sorts. Gross i.

Which is half the quantity sent out for Fort St. David.

N. Barlow.

R. Douglas.

(D. & C. 1734) (Page 92 & 94)

In July 1937, the surgeons again requested leave to take some medicines out of those designed for Fort St. David. They represented that their indents for medicines were so shortly complied with that year, that they were again forced to make this request. The supply for Fort St. David was much larger than for Fort St. George in proportion to the consumption (page 117). Then, they submitted a list, the first one of any length, that can now be traced in the Fort St. George records. The list deserves close study both on

account of the drugs and other requirements of the Hospital as well as for the quantities requisitioned. It may be remembered that these articles are only some out of those intended for Fort St. David and the supply for that place must have been double or treble these quantities and that Fort St. George, the headquarters on the coast with its bigger garrison and large number of factors and other employees must have been indenting annually and receiving drugs and other druggists' wares, somewhat in excess of the supplies sent to subordinate factors like Fort St. David.

To the Hon'ble  
Richd. Benyon Esq.,  
President & Governor, etc.,  
Council of Fort  
St. George.

Hon'ble Sir & Sirs,

Our Indent for Medicines is so shortly complied with this year, that we find ourselves again necessitated to trouble your Hon. etc., for leave to take out of those design'd for Fort St. David the undermention'd particulars, the supply for that place being much larger than ours in proportion to the Consumption.

|                   |     |      |      |
|-------------------|-----|------|------|
| Aq. Theriacal     | ... | lit. | ii.  |
| Emp: eacut 17 am. | ... | ld.  | ii.  |
| Diachyl simp      | ... | lit. | iv.  |
| Mellilot          | ... | lit. | iv.  |
| Paracels          | ... | lit. | i.   |
| Oxycroc           | ... | ld.  | ii.  |
| de ran 17-810     | ... | lit. | i.   |
| Ung. Basilic      | ... | lit. | iii. |
| Nervin            | ... | lit. | ii.  |

|                       |     |          |       |
|-----------------------|-----|----------|-------|
| Linim arecei          | ... | ld.      | ii.   |
| Bals Sulph. Ard.      | ... | oz.      | ii.   |
| Tereb                 | ... | ld.      | ii.   |
| Viride                | ... | oz.      | xiv.  |
| Rez Cord Peru         | ... | oz.      | i.    |
| Gum Guaic             | ... | lit.     | i.    |
| Tereb Venet           | ... | lit.     | ii.   |
| Commun                | ... | lit.     | iv.   |
| Pill Russi            | ... | oz.      | ii.   |
| Rud                   | ... | oz.      | iv.   |
| Sem. Carui            | ... | lit.     | ii.   |
| Bolus Verus           | ... | lit.     | i.    |
| Elect Linitu          | ... | lit.     | i.    |
| Tol Senna             | ... | lit.     | v.    |
| Hord Gallic           | ... | lit.     | x.    |
| Styptic Eaton         | ... | lit.     | i.    |
| Spir. Corn. Cere P se | ... | oz.      | viii. |
| Lavend C.             | ... | oz.      | viii. |
| Vin Rectif            | ... | ld.      | ii.   |
| Sal Ammon             | ... | lit.     | i.    |
| Menth                 | ... | lit.     | ii.   |
| Nitr. dulc            | ... | ld.      | i.    |
| Elix Vitriol          | ... | ld.      | i.    |
| Proprietat            | ... | ld.      | i.    |
| Ol. Terebinth         | ... | lit.     | ii.   |
| Ol. Menth.            | ... | oz.      | i.    |
| Tinct. Castor Russ    | ... | ld.      | i.    |
| Sacra                 | ... | lit.     | iii.  |
| Merc. dulcis          | ... | oz.      | xii.  |
| Calomel               | ... | oz.      | xii.  |
| Lap: Infernal         | ... | oz.      | ii.   |
| Sal Mirab Glaub       | ... | lit.     | ii.   |
| Syr. Diacod           | ... | lit.     | ii.   |
| Pulv. Corn. Cerobal   | ... | lit.     | x.    |
| Vials                 | ... | 3 Groce  |       |
| Potts                 | ... | 4 Dozens |       |
| Pill Boxes            | ... | 2 papers |       |
| Thread                | ... | lit. B.  |       |
| Flannel               | ... | 5 Yards. |       |

We are  
Hon'ble Sir & Sirs  
Your most Obed. Hble Servants,  
Nathaniel Barlow,  
Robert Douglas.  
(D. & C. 1727, p. 119.)  
Fort St. George,  
July 27th, 1737.  
By 1739, the procedure for  
sending indents for stores and

medicines seems to have been regularised. In the record of a Consultation dated 24th January 1739, the following entry is noted:—"Indent for stores and medicines for 1740 signed; as are several other papers for England". (Page 28). Again, the Consultation on 14th January 1740, mentions "Indents to England for medicines for 1741 signed". Indents were approved and signed by the whole council. It is evident that indents were sent well in advance, being forwarded from Madras in January of every year for the medicines expected in the course of the next year. In 1740, medicines etc., received from England by the ship Colchester on 30th September, probably in response to the indent sent in January 1739.

#### Some Diseases, Treatments and Sea Voyages for the Recovery of Health.

*Scurvy* figures prominently in the early records of the Company. On 7th June 1725, the Council granted the request of Captain James Winter who represented that one of his soldiers consigned for Bengal was so dangerously ill of the Scurvy that it is precarious to carry him further. The Captain also begged leave to *admit the patient to the Hospital immediately* with a hope of recovery. (D. & C. 1725, pp. 87 and 92). In July 1736 James Montgomery Captain of the ship gave as reason for his footing into the Fort of Madras the illness of his sailors "I have now at this time 24 foremastmen and 2 quarter-masters with this Scurvy, not able to help them-

selves; besides 13 that can but just walk the deck and expect they will lay down every moment by other distempers which obliges me to put into recover all their health". (D. & C. p. 99). William Jodson, Captain of Royal George, also represented in June 1738, that most of his sailors were in a miserable condition with Scurvy, that they recovered on touching at Batavia but relapsed again and he therefore put into Madras for fresh provisions.

*Dysentery*.—Edward Brackstone petitions the Council in September 1728:—"Having laboured under a very severe *flux* for this twelve months past, or upwards and finding myself much worse in the monsoon than in the other part of the year, I am apprehensive of the fatal consequence that may attend the approaching one". (D. & C. 1728, p. 128).

*Disorder of Liver*.—Petition of Mr. Rush, Surgeon of the *Cadogen*:

President and Council,

I am unhappily indisposed with the *disorder in my liver, a distemper which I understand is frequent and sometimes fatal in this place*. I have been advised for the recovery of my health to enter into a *Mercurial Course* which will prevent my going on board our ship the *Cadogen* with safety. I therefore humbly desire your honour to consent to my staying ashore for the recovery of my health.

John Rush.

(D. & C. 1731, p. 31).

No reference to *Venereal diseases* is found till the year 1742. On 16th August of that year, Doctors Barlow and Munro, submitted "As the number of *venereal patients* in Company's Military servants in the Hospital to whom large quantities of medicines are for that purpose exhibited are always considerable, we beg leave when such medicines for the use of the Hon'ble Company that are under our care are expended, we may petition for a supply from these .....

The Doctors of the Hospital also seem to have attended on some accident cases from the town. Gode Ankennah represented to the Governor on 16-11-1724 that he was called out by some persons who gave several wounds on his belly, and his breast and thinking that they had killed him, left him on the road. The Governor ordered Doctor Pitchier to dress the wounds of this man and the Doctor told him that if he had stayed but four hours longer without a Doctor he would have been a dead man- (D. & C. 1724). p. 202.

It seems to have been a fashion even in those days to recommend a sea voyage for health as well as for the cure of many diseases. In 1711, Richard Skingle of Madras requested permission to go to England "Finding my illness to increase very much upon me as the Doctor can inform you, and but little or no hope of recovery."

Francis Hastings sent in the following application to the Governor:—

"Having very lately been dangerously ill that my physician almost despaired of my life and being now in such a weak state of body that unless I go for England very speedily I am apprehensive it will be very much endangered, I desire your Honour etc. to permit me to take my passage on the 'Marlborough'" (D. & C. 1721, p. 190).

Issac Pyke also petitioned:

"Labouring under a great indisposition in so much that his illness later confined him above 9 weeks to his chamber and now before he is recovered it return again much the same manner as before, wherefore for the recovery of his health and preservation of his life he prays your Honour etc. to permit him to return to England." (D. & C. 1722, p. 166).

In July 1734, Thomas Weston petitions that he has been afflicted for the last 12 months with a distemper which has deprived him of the use of all his limbs and rendered him incapable of doing his duty. He adds "That after the application of all the usual remedies the distemper still increases so much upon me that the *Physicians here have consulted and agreed that a change of climate is absolutely necessary.* I therefore apply to your honour for leave to return to England upon the first conveyance in order to recover my health." (D. & C. 1734, p. 93).

In June 1740, Eden Howard petitioned to leave India—"Having during my stay in India felt the hot season every year troublesome to me and sometimes so affected by it that I have not been able to do my office in the manner I could wish. And this year in particular I have felt the bad effects of it in such a manner that gives me some apprehension I cannot stay in India consistent with my health and duty of my office."

Even China and Bengal or at least voyages to either of these places, appear to have been recommended for the recovery of health.

William Martin petitioned the Council in June 1737 that he was labouring under severe illness for several years, that he was apprehensive of the approaching land wind season being fatal to him and requesting permission to go on the *Royal Guardian* to China. He also adds that the physicians of Madras gave no hope of recovery from the ill-state of health and suggested that a change of air may be a means to recover his former state of health (D. & C. 1737, p. 90).

In September 1737, Augustus Brunton "indisposed for some time and the doctors advising for change of air," petitioned to go on the first ship to Bengal. (D. & C. 1737, p. 137).

#### Cases of Medico-Legal Interest:

A few instances of medico-legal interest may be added here. In August 1737, there was what may be said to be the first application

for work men's compensation. Henry Fegge requested a certificate that the damage he sustained, viz., the loss of the first joint of his thumb of his right hand, due to a gun shot injury, depriving him of the proper use of his hand, occurred in the service of the Company. Francis Akeman who came out as a soldier lost his hearing without any hope of recovery. As he was disqualified for any calling or any other business, he was struck off from the Military Role and was put on the list of pensioners from July 1738.

A case of poisoning came up before Emerson, Chief Justice of the Choultry in 1726. A woman slave attempted to poison a whole family. The poison has actually been given. "But operating very violently, quickly discovered itself and the effect was prevented by immediately administering proper emetics." (D. & C. 1726, p. 168).

Release from prison was prayed for and allowed in case of severe illness. Markrishna petitioned as follows in 1722:—"Being under confinement at the Fort, and not having conveniences proper to take the necessary physick for recovery of his health"... "Having been under confinement near 14 months, has occasioned him to be afflicted with *barbeers and bloody flux* which distempers if proper medicine are not applied, in a short time may probably prove mortal...he implores you, that he may be at his own house and use the best methods for the recovery of his health, it being impossible to take any physick where he now is." (D. & C. 1722, p. 162).

The following extracts deal with a mental case kept under observation of the physicians at Madras who finally submitted their reports and certificates:—

The President produces a letter which he received yesterday (6th April 1720) from Mr. Thomas Jenkinson who has been some time in a state of lunacy: the said letter being read, is entered after this Consultation, and being considered particularly that passage wherein he asserts his perfect recovery, and capacity to manage his own affairs, The Board recollecting that it might have been wrote in a lucid interval, as had been his case before, immediately sent for Messrs. Robson and Pitchier, the H. Comp's two surgeons, who attending the Ward, were in the Sev'l needfull respects question'd concerning him, and after having assign'd severall physicall reasons for his being not yet reinstated in a sound body and mind, they gave their final solution to the purpose, that he could not be yet perfectly recovered, because obnoxious to relapse, as he had done more than once before, notwithstanding he was to all appearance 'compostmentis. "It is therefore Agreed to take no further notice of this affair till the Surgeons report his perfect Recovery with this exception howev'r that the present Trustees may discourse him about his making choice of others in their room, they being willing to resign them, trust to make him easy, w'ch. when they have done they may report his answer. (D. & C. 1720, p. 55). At a later Consul-

tation dated 20th July, the Council ordered that all the Surgeons in the place do give their opinions in writing relating to Mr. Jenkinson's distractions that if he find there is no probability of his recovery, we may send him to Europe by first conveyance. (D. & C. 1720, p. 126).

On 30th July 1720, Andrew Pechier sent the following report:—Hon'ble Sr. &c'a.

On the 10th of January last, Mr. Tho's Robson late Dec'd. and I were sent for to visit him. We found him afflicted w'th a Mania or Malancholly madness having a deprivat'n of Imaginat'n and Judgement Accompany'd w'th great rage and Anger but without Fever.

We administer'd to him from time to time what is practicable in those cases as *Emeticks Cephalicks* &c'a hav'g had several Intermissions and Chiefly towards the New Moon at w'ch time he acts and Speaks w'th a great deal of Vivacity as is accustomed w'th those people in that deplorable Condition.

He never could be perswaded to take Phys'k voluntarily but always oblig'd to have assistance of two other men being of Opinion that the Change of Climate may contribute much towards his recovery Because these Southerly Monsoons affect the Nerves and animall Spirits in great degree I wish he may be able to Justify the same.

Andrew Pitchier.  
(D. & C. 1720, p. 138).

July the 30th 1720.

Then follows the certificate by other Doctors of the place:—

Having visited Mr. Thomas Jenkenson for some days and being inform'd by the Surgeon that now attends him of the method after w'ch he was treated since the beginning of his illness, we believe that going to a cold country (w'th himself earnestly desires) may contribute much to restore him.

Hon'ble Sr. & Ca.

Your most humble Servants.

Dun. Munro.

Hugh Hopkins.

James Chatelier.

(D. & C. 1720, pp. 138 to 139).

Finally on 8th August 1720, the Council considered the case and ordered as follows:—"The Surgeons deliver in their report of Mr. Jenkinson's distractions (as enter'd after this Consultation) setting forth that his going into a cold country may probably contribute to restore him. Wherefore it's ordered that he be sent upon the *Hanover* and that his trustees provide every thing necessary for the voyage."

#### The Hospital buildings and the Surgeons' lodgings.

Though the buildings were completed in the 2nd decade of the 18th century, frequent repairs, major or minor, had to be done now and then. In 1726, the Paymaster submitted a report

of the sundry small repairs necessary for *Doctors' lodgings*.

Sir,

Dr. Ramsay having complained to me that the *Surgeons' lodgings at the south end of the Hospital* being so much out of repair that he cannot come into them and therefore he is obliged to be at the expense of house rent, I thought it my duty to take the head carpenter and see what is necessary to be done to it and report the same to your honour as near as we can with a calculate of the cost which is as follows:—

There are seven windows and nine doors which want to be all new painted. Five of the said windows want also to be new rattanned to do all which will take up

| I. For painting.—                | Pags. |
|----------------------------------|-------|
| Linseed oil, five gallons.       | 2 28  |
| White lead, one mond...          | 1 27  |
| Indigo, five viss                | 0 35  |
| Mooches                          | 1 14  |
| Red earth, four viss             | 0 8   |
| II. For rattanning five windows— |       |
| Rattans two bundles              | 2 24  |
| Rattan cooly                     | 0 30  |
| Total Pags                       | 9 22  |

The old stairs are entirely rotten and useless, must be taken away to make which good again and to give a small repair to the well, cookroom and necessary house will be used.

|                                | Pags. |
|--------------------------------|-------|
| Red wood for the well.         | 1 0   |
| Some plank for the stairs etc. | 12 0  |

|                                                                                             |     |    |    |
|---------------------------------------------------------------------------------------------|-----|----|----|
| Smiths, carpenters, bricklayers, coolis and boys                                            | ... | 10 | 0  |
| Chinam, jaggery pots, etc. for plastering and white washing                                 | ... | 3  | 0  |
| Emptying the necesary house.                                                                | ... | 0  | 20 |
|                                                                                             |     | 26 | 20 |
| Total                                                                                       |     | 35 | 6  |
| The painting of other surgeons lodgings at the north end will amount to much above the same | ... | 7  | 4  |
| White washing about                                                                         |     | 3  | 0  |
|                                                                                             |     | 10 | 4  |
| Total                                                                                       |     | 45 | 10 |

(D. & C. 1726, p. 21.)

In the accounts for extraordinary expenses for February 1726, there is an entry under repairs to fortifications, etc.

Hospital and Doctors' lodgings (p. 20).

|                                    |         |
|------------------------------------|---------|
|                                    | Pags.   |
| Palmeras and Rippers               | 2 0 0   |
| Teak plank 1                       | 3 0 0   |
| Nails and carpenters               | 2 0 0   |
| Chenam 175 Parra                   | 12 8 0  |
| Wall bricks 2550                   | 1 18 0  |
| Paving do 3150                     | 4 18 0  |
| Tyles 2000                         | 0 18 0  |
| Cadaci gram for brick layers wages | 21 27 0 |
| Total                              | 48 1 0  |

"Repairing the south lodging of the hospital Pags. 40-30-20" Next year (1727) according to the orders of the council, the surveyor of the works reported on sundry repairs wanting in Company's buildings. The portion relating to the hospital is extracted below :—

"In the new house and hospital, the chinam and pavements both within and without want mending and the doors and windows have not been painted for many years by which the wood has suffered very much. On this occasion, we beg leave to remark that it would tend very much to preserve yearly or almost every two years. The necessary repairs in this head will cost as follows;

Estimates for chinam, clay, sand, and wages, the buildings in general to paint the doors, windows and rattans etc, etc. given here.

Again in January 1733, a report was submitted on the neglected state of the buildings:

In the accounts for March 1738, the following entry is recorded under repairs to fortifications :—

Doctor Douglas' Apartment.

|           |     |   |    |    |
|-----------|-----|---|----|----|
| Materials | ... | 6 | 31 | 42 |
| Workmen   | ... | 7 | 11 | 20 |

In the account for April 1738, the extraordinary expense is explained as due to various things amongst which is mentioned :

Repairs to Doctors' lodgings.

|                                            |         |
|--------------------------------------------|---------|
| Doctor Barlow and Douglas their apartments | Pags.   |
|                                            | 7 20 19 |

In May 1738, there is an entry : Doctor Barlow's lodgings 3 21 59

Similarly the extraordinary expense in December 1738, was due to : "Doctor Barlow's lodgings. Workmen and materials Pags. 4 13 60

In the year 1739, in the accounts for October, an entry is made indicating repairs to the hospital and buildings, costing Pags 23 10 0

Accounts and audit of the Hospital expenditure.

From September 1724, there appears a new heading in the monthly statement of accounts by the Paymaster.—"Hospital charges."

|                                                      |         |
|------------------------------------------------------|---------|
| Hospital Charges in September read in October, Pags. | 32 19 0 |
| Hospital Charges in October read in November, Pags   | 44 31 0 |
| Hospital Charges in November read in December, Pags  | 93 19 0 |

(Of this amount the extraordinary charges amount to Pags. 50 on account of arrears paid to Doctor's mates).

The Council ordered Randall Fouke to look through Paymaster's accounts and report what might be done immediately towards retrenching the charges, conformable to the company's prescriptions (D. & C. 1274, p. 121).

A number of detailed criticisms or comments were made on different items of which the following concerned the hospital accounts:—

- 1 One of the Sergeants of the three companies was *steward of the Hospital*. So, it was suggested that his pay be debited to Hospital and his monthly allowance fixed by the Board.
2. The heads of charges were subdivided according to the appropriations to a particular use.
3. Our Honourable Masters complain of large salaries to Supervisors of buildings and "others" ..... and of bazaar physick and other articles. The "others" referred to, were Doctors mates and steward of the hospital. It was proposed to save 50 pags. per month from these items.
4. A reference was made to the expenses on peons, etc. The Governor and Council, Secretaries, Ministers, *Doctors Servants* stood always much the same but in the year 1707 Mr. Frazier happened

to be suspended so there was no second but one Doctor which might occasion some difference.

In the same year, another alteration was made on 4-9-1724. "The Doctor's mates having been in the Military Role as Sergeants and now dismissed; ordered that their pay be advanced 2 pagodas each (D. & C. 1724, p. 140).

Even as early as 1726, there was trenchant criticism on hospital expenditure. Ways and means were devised for reducing the expenditure as the following comment indicates:—

"The president represents the Board that upon reading the particulars of the article of charges of Hospital, he apprehends there are several of them too large and others unnecessary and ought to be reduced and discontinued; which being taken into consideration and the several particulars again read and enquired into, it was represented that the surgeon who has the immediate direction of the hospital always insists that the present charge is necessary for entertaining and recovering the sick and that no reduction can be made of it. "Ordered that whereas it hath been for some time the custom for one of the surgeons to have the immediate care of the hospital solely, they do in future act each 6 months by turns that by their acting thus, interchangeably, we may make the experiment whether they cannot reduce the charge of his hospital lower than the other, which it is

believed out of emulation to recommend themselves, they may do" (D. & C. 1726, p. 137).

Fort St. George charges other settlements for dieting and treating patients. In August 1728 there is an additional entry—Bengal Presidency—and the explanation adds the following information.—"Paid the Steward of the Hospital by order of the Consultation, his bill for victualising the Bengal soldiers from the "Compton" while they remained sick ashore in the hospital here,; Pags. 18-18-0" (p. 133). Again in August 1729 there is an entry—Bengal Presidency. "Paid Steward of the hospital's bills for victualising 5 of Grantham's soldiers for 16 days while they were ashore here, Pags. 5-12-0" (p. 85). In 1734 there is an entry under extraordinary expenses—"Paid Doctor's mate for hospital charges on a Bengal soldier, 1-14-32". Another entry of interprovincial interest: "Bengal Presidency—Entertainment of sundry sick soldiers belonging to that place in the Hospital, 4-24-50" There are some other accounts connected with medicines sent or coolly hire for boxes of medicines to Fort St. David or allowance to one Mr. Hague while he remained at Fort St. George, "he being appointed surgeon of Bencoloon."

The following tabular statements prepared from scattered sources, may serve to give the reader an idea of the monthly expenditure and the tendency of the Hospital Charges to increase steadily from year to year.

## Paymaster's Accounts.

HEAD OF ACCOUNT:—Hospital Charges.

PAGS.

|       |                                                                                       |     |     |    |    |
|-------|---------------------------------------------------------------------------------------|-----|-----|----|----|
| 1725. | Accounts for February read in March 1725                                              | ... | 52  | 29 | 0  |
| "     | March " April                                                                         | ... | 54  | 8  | 0  |
| "     | April " May                                                                           | ... | 54  | 31 | 0  |
| "     | May " June                                                                            | ... | 52  | 6  | 0  |
| "     | June " July                                                                           | ... | 53  | 15 | 0  |
| "     | July " August                                                                         | ... | 64  | 30 | 0  |
|       | (This includes extraordinary charges of 10 pags. paid to Mr. Ramsay).                 |     |     |    |    |
| "     | August " September                                                                    | ... | 63  | 23 | 0  |
| "     | September,, October                                                                   | ... | 166 | 27 | 0  |
|       | (Extraordinary charges for quilts etc. 90-11-60)                                      |     |     |    |    |
| "     | November,, December                                                                   | ... | 65  | 35 | 0  |
| 1726. | December 1725                                                                         | ... | 61  | 26 | 0  |
| "     | January 1726                                                                          | ... | 48  | 32 | 40 |
| "     | February                                                                              | ... | 51  | 31 | 0  |
| "     | March                                                                                 | ... | 42  | 35 | 0  |
| "     | April                                                                                 | ... | 38  | 20 | 0  |
| "     | May                                                                                   | ... | 42  | 32 | 0  |
| "     | June                                                                                  | ... | 42  | 24 | 0  |
| "     | July                                                                                  | ... | 41  | 28 | 0  |
| "     | August                                                                                | ... | 43  | 9  | 0  |
| "     | September                                                                             | ... | 42  | 18 | 0  |
| "     | October                                                                               | ... | 41  | 0  | 0  |
| "     | November                                                                              | ... | 45  | 13 | 0  |
| 1727. | December 1726                                                                         | ... | 45  | 22 | 0  |
| "     | January 1727                                                                          | ... | 43  | 16 | 0  |
| "     | February                                                                              | ... | 44  | 9  | 0  |
| "     | March                                                                                 | ... | 43  | 0  | 0  |
| "     | April                                                                                 | ... | 42  | 10 | 0  |
| "     | May                                                                                   | ... | 103 | 30 | 70 |
|       | (Of this Pags. 68-3-70 was due to quilts, banian coats, drawers, shirts, caps, etc.). |     |     |    |    |
| "     | June                                                                                  | ... | 46  | 27 | 0  |
| "     | July                                                                                  | ... | 48  | 10 | 0  |
| "     | August                                                                                | ... | 40  | 12 | 0  |

|              |              | PAGS. |         |
|--------------|--------------|-------|---------|
| Accounts for | September    | ...   | 38 33 0 |
| "            | October      | ...   | 43 30 0 |
| "            | November     | ...   | 40 4 0  |
| "            | December     | ...   | 40 10 0 |
| 1728.        |              |       |         |
| "            | January 1728 | ...   | 42 5 0  |
| "            | February     | ...   | 44 22 0 |
| "            | March        | ...   | 41 31 0 |
| "            | April        | ...   | 40 3 0  |
| "            | May          | ...   | 44 2 0  |
| "            | June         | ...   | 66 23 0 |
| "            | July         | ...   | 43 34 0 |
| "            | August       | ...   | 46 1 0  |
| "            | September    | ...   | 47 9 0  |
| "            | October      | ...   | 42 7 0  |
| "            | November     | ...   | 46 28 0 |

Yearly Expenditure under the head "Charges Hospital"  
As per books for each year ending April.

| Year |     |     | Pags.     |
|------|-----|-----|-----------|
| 1725 | ... | ... | 471 1 15  |
| 1726 | ... | ... | 769 35 30 |
| 1727 | ... | ... | 838 30 33 |
| 1728 | ... | ... | 826 19 9  |
| 1729 | ... | ... | 870 0 53  |

(The increase in this year is occasioned by a greater number of sick in the hospital).

|      |                                                   |     |             |
|------|---------------------------------------------------|-----|-------------|
| 1730 | ...                                               | ... | 784 21 12   |
| 1731 | ...                                               | ... | 896 26 27   |
| 1732 | ...                                               | ... | 840 17 18   |
| 1733 | ...                                               | ... | 1,025 24 20 |
| 1734 | ...                                               | ... | 872 35 40   |
| 1735 | ...                                               | ... | 1,097 19 25 |
| 1736 | ...                                               | ... | 1,064 7 10  |
| 1737 | ...                                               | ... | 984 9 20    |
| 1738 | The increase of 152-32-56 is explained as due to: |     |             |

(1) Medicines more this year than last ... 67 14 50

(2) Clothes for sick people this year ... 85 18 6

152 32 56

|      |     |     |           |
|------|-----|-----|-----------|
| 1739 | ... | ... | 1137 6 46 |
|      | ... | ... | 1114 29 0 |

## Neurosyphilis—A Clinical Study.

By P. KUTUMBIAH, B.A., M.D., M.R.C.P. (LOND.),

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Neurosyphilis is not such a rarity in India as is made out in modern text-books on medicine and in current medical literature. It would be strange if it were in fact. Syphilis is very common in all the big towns of India and there is no dearth of nervous cases in the out-patient clinics attached to the various big general hospitals. In other countries where both the above diseases are common, syphilis stands first in frequency and importance among the known causes of organic disease of the nervous system. So it would require very strong evidence to prove that in India alone this is not the case. Syphilitic disease of the central nervous system constitutes a group of clinical manifestations of limitless variety. The disease may resemble in its clinical aspect almost any neurological disease or syndrome. "In neurology there are no clinical entities exclusively syphilitic". To substantiate a diagnosis of neurosyphilis consideration must be given to age, antecedent history, onset and evolution of symptoms, clinical examination and laboratory findings of the blood and cerebrospinal fluid. Correct history is very difficult to obtain particularly in connection with venereal diseases, mostly due to a false sense of

modesty. The study of neurology is still in its infancy in India, at any rate in South India, and many cases of nervous disease are imperfectly diagnosed. Facilities to obtain blood and cerebrospinal fluid findings are at present available in South India in two or three organised centres only. But wherever the available clinical material is carefully scrutinised and studied with all the available laboratory aids it is becoming more and more evident that a good number of our neurological cases owe their origin to syphilis.

The incidence of neurosyphilis has been variously estimated by different groups of workers at different periods in different countries. Correct statistics as to the incidence of the various types of neurosyphilis are even now difficult to obtain. The most authoritative figures on the course of the disease comprising a fairly large number of cases are those published by Mattanschek (1920). 4,134 syphilitics were observed for a period of 22 years (1890-1912). Of these 113 (2.77 per cent) developed cerebrospinal syphilis; 132 (3.2 per cent) developed tabes; and 198 (4.7 per cent) developed G. P. I. According to Collier and Adie (1933) cerebrospinal syphilis

occurs in about 4 per cent of all persons who acquired syphilis and G.P.I. in about 5 per cent of untreated syphilitics and in about 1 per cent of those who had thorough treatment. No figures are given as to the incidence of tabes. Macrae (1935) cites the John Hopkins statistics. Out of 16,562 syphilitics, 201 (about 1.2 per cent) were noted to be suffering from tabes. The above statistics exclude those cases of "meningeal reaction", which commonly occurs in those suffering from secondary stage of syphilis without any nervous symptoms. This is said to occur in 80 per cent of syphilitics.

Statistics with regard to the incidence of the various types of neurosyphilis are very scarce in Indian medical literature. There are a few scattered references to the incidence of tabes and G.P.I., but very few with regard to the other types of neurosyphilis. According to the Madras General Hospital reports, the incidence of neurosyphilis among the syphilitics attending its venereal clinic for the years 1934 and 1935 is given as 4.5 and 3.6 per cent respectively. Rajam (1930) in an article entitled "Syphilis in Madras" gives the percentage of neurosyphilis as 2 per cent of the total number of syphilitics. The statistics of the venereal clinic of the King George Hospital, Vizagapatam, gives the incidence as approximately 7 to 9 per cent among the male syphilitics. The majority of the cases are of cerebrospinal type; tabes and G. P. I. are only occasionally

met with. Manohar (1935) in the course of a detailed examination of 882 autopsies found evidence of central nervous infection in 19 per cent of the syphilitics. The incidence of G. P. I. and tabes in Indians is very much doubted. So the following references with regard to the incidence of these diseases should be interesting. Shaw (1926), Superintendent, Central Lunatic Asylum, Poona, writes: "I have seen 20 cases of G. P. I. among Indians. There can be no doubt that G. P. I. exists among Indians, though it is nothing like so common as it is among Europeans." Prasad (1926) during six years of venereal practice in Karachi came across only two cases of tabes, one in a Hindu and the other in an Indian Christian. He refers to five cases of G. P. I. in the Mental Hospital, Agra. Fraser (1934) from his experience of Burma writes: "The classical form of G. P. I. is relatively common in Burma, accounting for 6 to 19 per cent of admissions into the mental hospital, between the years 1931 and 1933. According to the report of the Mental Hospital, Madras, there were 36 cases of G. P. I. undergoing treatment in the hospital in 1936. This gives a percentage incidence of 2.7 of its total admissions. The Mental Hospital, Waltair, reports no cases under treatment in the year 1936. The nationality of these cases is not noted. Vad and Kulkarni (1929) report 16 cases of tabes from Bombay, by far the largest number ever reported in Indian literature, of which five were treated by malarial therapy.

Here also the nationality of the patients is not noted except in one instance—a Chinese.

This article is based on a study of 50 cases of neurosyphilis investigated and treated in the medical wards of King George Hospital, Vizagapatam. All the patients were Indian males. Out of a total admission of 6,370, 392 were neurological cases and of these 75 were cases of neurosyphilis. The percentage of nervous cases to the total admissions worked out to 6.5 and the proportion of neurosyphilitic cases worked out to 1.2 per cent of the total admissions and 19 per cent of the neurological cases. These statistics are not a true indication either of the prevalence of neurological cases or of

neurosyphilis, because only cases which are interesting and worthy of investigation are admitted into the wards and all the others are treated as out-patients due to want of accommodation.

It is now generally conceded that all types of neurosyphilis are meningo-vascular in origin and the classification of neurosyphilis into primary meningo-vascular and primary parenchymatous syphilis is not supported by serological evidence. But for clinical purposes it is still convenient to describe cases of neurosyphilis under certain types. The 50 cases which form the material of this study when analysed fall under the following heads:

|                              |     |                            |     |    |
|------------------------------|-----|----------------------------|-----|----|
| I. Cerebral types (17)       | (1) | Meningitis                 | ... | 6  |
|                              | (2) | Cerebral endarteritis      | ... | 5  |
|                              | (3) | Cranial nerve affections   | ... | 6  |
| II. Spinal types (25)        | (1) | Meningitis.                | ... | 1  |
|                              | (2) | Meningo-myelitis (chronic) | ... | 15 |
|                              | (3) | (acute)                    | ... | 9  |
| III. Cerebrospinal types (2) |     |                            |     | 2  |
| IV. Tabes dorsalis (4)       |     |                            |     | 4  |
| V. G. P. I. (2)              |     |                            |     | 2  |
| Total ...                    |     |                            |     | 50 |

I. *Cerebral types*. These were the earliest manifestations of neurosyphilis in this series. They occurred within a year of the infection. The shortest period intervening between the infection and the onset of the disease was three months and the longest one year. The age incidence was between 20 and 30 years. The oldest patient was 40 years of age. These cases are divisible into three clinical varieties:

(a) *Meningitis*: The period of onset in this type was generally a few months from the date of infection. The cerebrospinal fluid showed marked increase in cells. Total proteins were increased, including globulin. No change was noticed in chloride and sugar content. Both blood and cerebrospinal fluid were strongly positive for W. R. The cellular increase varied from 10 to 275 cells per c.mm. The cells were mostly

lymphocytes and in a few cases plasma cells were also present. The protein content varied from 20 to 150 mgms per cent. In most of these cases there was involvement of the cranial nerves. The nerves involved in the order of their frequency were, the seventh nerve in four cases, the third in two cases, and the sixth in one case. The presenting complaint was headache or some cranial nerve paralysis usually the seventh nerve. The headache was severe with nocturnal exacerbation. All these cases responded well to treatment with lumbar puncture and the usual antisyphilitic treatment.

*Case I.* P.A. 35, male Hindu—admitted for headache and vomiting. History of syphilis three months back. Pupils react sluggishly to light. Seventh nerve on the right side paralysed, hearing slightly diminished in the right ear. Upper extremity jerks normal. K. J. and A. J. normal. Plantar reflex flexor, abdominal normal. Blood Wassermann reaction + + C. S. F. Wassermann reaction + +. 275 cells per c. mm. Protein 150 mgms per cent. Globulin (N. A.) +.

(b) *Cerebral endarteritis*: This type commonly manifested itself as a slowly evolving hemiplegia. Most of the patients were young adults. There was no clinical evidence of disease of the cardiovascular or of the renal system. Evidence of meningeal involvement was not present in all cases. Generally there was an increase in the total proteins. Globulin

was present in all cases and the Wassermann reactions of the cerebrospinal fluid and blood were strong positive. Cellular increase was not marked in most cases. All the cases responded well to antisyphilitic treatment but the hemiplegia was not completely recovered from.

*Case II.* M. L. 24 years, male Hindu—admitted into the ward for persistent headache and weakness of the right side of the body. History of infection eight months back. Had a course of treatment for it in the hospital. Cranial nerves normal. Grip weak in the right hand. B. J., T. J. and S. J. brisk and K. J. and A. J. exaggerated on the right side. Abdominal reflexes lost on the right side. Plantar reflex extensor on the right side. No sensory changes. Cerebrospinal fluid clear, 38 cells per c. mm., protein 75 mgms per cent, globulin (N. A.) positive, chlorides 710 mgm per cent. Sugar 33.33 mgm per cent. Langes curve 112332100, W. R. + +, Blood W. R. + +.

(c) *Cranial nerve paralysis*: As noticed above, these generally occur in association with meningitis. But there were a few cases of cranial nerve involvement without any evidence of meningitis in this series.

II. *Spinal types*.—These cases can be divided clinically into two varieties:

(a) *Meningitis*: It is rare for the meninges alone to be affected and when this occurs it usually

affects the cervical region. The C8 and D1 segments are involved. The small muscles of the hand are wasted, resembling cases of progressive muscular atrophy. Here sensory changes are noticed early and are persistent. Radiating pain round the neck, over the shoulders and down the upper limbs occur. These changes are followed by progressive atrophy of the muscles supplied by the corresponding anterior roots. Compression ischaemia of the cord leads to progressive spastic paraplegia. There was only one case of this type in this present series.

*Case III.* M.R. B. 30 years, male Hindu—admitted for pain and stiffness of the neck and paresis of all limbs. No definite history of infection, lost two children soon after birth. Rigid neck, both upper extremities paralysed and the lower extremities paretic, muscles of the forearms wasted, especially the extensors, slight wrist drop, the intrinsic muscles of the hands, wasted, ulnar nerves on both sides not thickened, B. J. and T. J. absent, S. J. sluggish, K. J. and A. J. + +, ankle clonus present on both sides, pupils dilated, equal on both sides, react sluggishly to light, C. S. F. xanthochromic, 7 cells per c. mm., albumin 600 mg. per cent, globulin N. A. + +, sugar 94.3 mg. per cent, chlorides 688 mg. per cent, W. R. + +, Blood W. R. negative. X-ray of cervico-dorsal spine: no caries of the spine, no cervical ribs.

(b) *Meningo-myelitis*.—This was the commonest type of neurosyphilis met with in our clinic.

The period of onset of the symptoms varied from one to five years from the date of infection. The condition was either acute or chronic. The acute forms were less common than the chronic ones. In this series there were nine cases of the acute variety. The lesion appeared to be more vascular than meningitic. The signs and symptoms were those of a transverse lesion of the cord and developed during the course of a few hours to days. Generally there were promonitory symptoms—pains in the back and in the limbs and in some cases paresis of the lower extremities. Then complete paralysis of the lower extremities set in suddenly. The paralysis was flaccid at the commencement, with loss of knee and ankle jerks but with the plantar reflex extensor, and gradually became spastic during the course of a few weeks. Sensory changes were marked below the level of the lesion from the onset. All forms of sensation were lost. The bladder was invariably involved requiring repeated catheterisation. In some cases the rectum was also involved. The C. S. F. in all cases showed an increase in the total proteins—the amount varying from 35 mgms to 400 mgms per cent. In four cases it was over 100 mgms and in one case it was 400 mgms. Globulin was present in all cases. The cells were not increased proportionately to the proteins. The cell count varied from 1 to 12 per c. mm. This "protein-cell dissociation" was noticed in six out of the nine cases. In one case only the cell

count was 100 per c.mm. These cases did not generally respond well to antisyphilitic treatment and generally died of bed sores or bladder infection. In a few cases where the lesion was not severe the condition passed on to the chronic variety with spastic paraplegia. The sensory symptoms cleared up and bladder control was regained. Malarial treatment was tried on three patients and two of them, who were bedridden with paralysis regained the power of walking. The signs of spastic paraplegia however persisted.

The chronic forms were more common than the acute ones. There were 15 cases of the chronic variety in this series. There was a history of pain in the back, tenderness over the spine, shooting pain in the limbs or round the trunk for varying periods at the commencement. Cord symptoms appeared after an interval with weakness of the legs progressing to spastic paraplegia. Sensory signs were not so prominent as the motor signs. Bladder control was impaired at some period or other in the course of the disease generally at the commencement. The contents of the C. S. F. varied widely in these cases, depending probably on the duration of the disease. In five cases the protein, globulin and cell content were normal but in all these cases there was a definite history of syphilis and the blood and cerebrospinal fluid Wassermann reactions were positive. In the other cases the protein content of the C.S.F. varied from 20

to 50 mgms per cent. Globulin was present; and the cell count varied from 1 to 50 per c.mm. The Wassermann reaction of the cerebrospinal fluid was positive in most cases and in those cases where it was negative in the beginning it became positive after a provocative dose of N.A.B.

Besides the above two types, intermediate forms were met with. There was one case of monoplegia in this series.

The response of these chronic forms to antisyphilitic treatment was not very marked. The acute symptoms disappeared on treatment; bladder control was regained but the spastic paraplegia persisted.

*Case IV. Acute type:—K., 30 years, male Hindu—admitted with paralysis of both lower extremities. History of syphilis and gonorrhoea two years back. Had a short course of antisyphilitic treatment. Six months after exposure he had severe headache and reeling sensation. For the past one and a half months progressive weakness of his lower extremities and dribbling of urine. For the past three weeks confined to bed. Cranial nerves normal. Pupils equal, moderately dilated, react to light. B. J., T. J. and S. J. exaggerated. Abdominal reflexes lost. Lower extremities paralysed. Muscles of the lower extremities flaccid. K. J. and A. J. sluggish. Plantar reflex extensor on both sides Cremasteric reflex lost on both sides. All sensations, except light touch, lost*

below the umbilicus. Sphincters of both bladder and rectum affected. C.S.F. slightly xanthochromic. Protein 100mgms per cent, globulin N.A.++, chlorides 682 mg. per cent, cells 8 per cubic mm., W.R.++, blood W.R.++. After a few weeks the knee jerks and ankle jerks became exaggerated. This patient died in hospital two years after admission. Towards the end he developed extensive bedsores. Post-mortem examination revealed no infection of the bladder or of the kidneys. He was treated with malarial therapy with no improvement.

*Case V. Monoplegic form: P., 25 years, Male Hindu. Complaint— inability to use the left lower extremity. Cranial nerves normal. Pupils moderately dilated, equal and react sluggishly to light. B.J. and T. J. and S. J. brisk. Abdominal reflexes lost. Right lower extremity muscles slightly flaccid. Plantar reflex extensor. Left lower extremity completely paralysed. K.J. and A.J. lost. Plantar reflex extensor. All sensations duller on the left side as compared with the right. Sensation of heat and cold lost over the left leg and thigh. Posterior column sensation intact in both extremities. Denied all history of infection. C.S.F.: cells 30 per cmm., protein 50 mgms per cent, globulin N. A. +, chlorides 734 mgms. per cent, sugar 32.5 mgms per cent, W. R.++, Blood W. R.++. Later the K.J. and A.J. became brisk on the paralysed side. Sphincters of both bladder and rectum affected.*

*III. Cerebrospinal type:—* In this series there were two cases in which there was dissemination of the lesions. The clinical picture was that of disseminated sclerosis in one case.

*Case VI. Disseminated sclerosis form.—*Hindu male, aged 30; gave a history of syphilis five years back; gross ataxia present, gait ataxic; muscles not wasted; no tremors; grip poor; finger nose test—slight degree of ataxy; Rhomberg's sign positive; nystagmus present; speech slurring and indistinct; knee jerk and ankle jerk exaggerated on both sides; ankle clonus present. Plantar reflex extensor on both sides; abdominal reflexes lost in both lower quadrants; bladder control lost; sensations: cotton wool sensation slightly impaired over the extremities; joint sense, vibratory and other posterior column sensations normal. C.S.F.: protein 10 mgms per cent; globulin nil, sugar 54.1 mgms. W.R. strong positive.

*IV and V. G. P. I. and Tabes.—* These were formerly called parenchymatous syphilis. The existence of these types of neurosyphilis in oriental countries is very much doubted and two reasons are given for its supposed rarity.

The prevalence of malaria in oriental countries is thought to be antagonistic to the prevalence of these forms of neurosyphilis. Induced malaria is now the recognised treatment of G. P. I. and to a certain extent

of tabes. As we have mentioned, malarial treatment is beneficial in meningo-vascular syphilis also. Though malaria favourably influences the course of G. P. I. and tabes and to a limited extent meningo-vascular syphilis, we have not enough evidence to dogmatise as to whether the development of tabes and general paralysis are prevented in a malarial country. The available evidence on the other hand points to this assumption being not correct. Vizagapatam District is notoriously malarial and cases included in this study are all from this district. We have already quoted enough evidence to show that cases of G. P. I. and tabes occur in India. In this present series there were four cases of tabes and two of G. P. I. All that can be definitely asserted on the present available data is that G. P. I. and tabes are not so common in India as in western countries.

The second reason given for the rarity of these forms of neurosyphilis is that the neurotropic strain of *spirochæta pallida* is not common in oriental countries. Before this assumption is taken for granted the existence of a neurotropic strain of *spirochæta pallida* should be proved. Most authorities doubt the existence of the so-called neurotropic strain. Unless the existence of the neurotropic strain is proved beyond all controversy it is futile to assume that the supposed rarity of neurosyphilis is due to the rarity of the hypothetical strain in oriental countries.

There were 4 cases of tabes in this series. Definite history of syphilis was available only in one case. The age of the patients varied from 27 to 40 years. In the case of the patient aged 27 years, a history of syphilis 12 years back was definitely given. In all the four cases there was marked ataxy; the knee jerks and the ankle jerks were lost; there was loss of vibratory sense and impairment of joint sense, deep muscle sense and tendon sense in the lower extremities; loss of sensation to light touch over the nose and round the mouth and dulling of sensation to pin prick over the same area; a band of anæsthesia across the chest about the level of the nipple. The true Argyll Robertson pupils with fixity and miosis were not noted. But the reaction of the pupils was sluggish to light in two cases. There was no optic atrophy in any case. The cerebrospinal fluid was normal with regard to the protein, globulin and cell content in three cases and in one case the protein was 50 mgms per cent; globulin was present and cells were 24 per cmm. The Wassermann reaction of the blood and the cerebrospinal fluid was strong positive in all the four cases.

*Case VII*—R.V.G., 27 years, male Hindu, admitted for inability to walk for the past two years. Gave a history of syphilis and gonorrhœa twelve years back. Had a course of injections of N.A.B. Four years ago noticed weakness and pain in the joints. Rhomberg's sign positive. Marked in-co-

ordination present in both lower extremities. No tremors and twitchings of the muscles. Muscular power good. Deep reflexes lost in the lower extremities, normal in the upper extremities. Abdominal reflexes lost in both upper quadrants and brisk in the lower ones. Cremasteric reflex lost on both sides. Plantar reflex not elicited. Sphincters normal; sensation: light touch lost over the toes of the right foot and the dorsum of both feet a band of anæsthesia at the level of the nipples across the chest, joint sense lost over the lower extremities. Cranial nerves normal. Cerebrospinal fluid: protein 50 mgs per cent, globulin (N. A.) +, chlorides 702.5 mgs. per cent, sugar 54 mgs per cent, Lange's curve: 000233210. Cells 24 per cmm. W.R. + +, Blood W.R. + +. Fundi normal. Test meal: nothing abnormal.

*Case VIII.* B.M., 30 years, male Hindu. Giddiness and pain in the chest. No definite history of syphilis. C. N. S: K. J. and A. J. lost on both sides. Plantar reflex not elicited. Abdominal reflexes sluggish in the lower quadrants. B. J. T. J. and S. J. sluggish. Rhomberg's sign present. Gross loss of sensation of position by the heel and knee test, cotton wool sensation lost over the nose; Appreciation of pin prick dull over the same area. Sensation for cotton wool and pin prick lessened distinctly over a band passing right across the chest at the level of the nipples. Vibra-

tory sense lost below the knees. Posterior column sensibility impaired over the lower extremities. Pupils react to light but sluggishly. C. S. F: 2 cells per c. mm. Protein 15 mgs per cent. Globulin Nil. W. R. + +. Blood W. R. +.

There were two cases of G. P. I. in this series. One was aged 30 and the other 47. In both these cases the mental condition of the patient was one of apathy and depression. In both there was a history of syphilis but the exact date of infection was not ascertainable. Cerebrospinal fluid showed characteristic changes. Protein was increased to 35 mgms per cent in one case and to 40 mgms per cent in the other. Globulin was present in both cases. The Lange's curve reading in one case was 155532000 and in the other 4543332110. Wassermann reaction of the blood and of the cerebrospinal fluid were strong positive in both cases. Malarial therapy was done on one case but the patient did not stay long enough in the hospital to note the effect on the course of the disease.

*Case IX.* L. V., 47 years, male Hindu. Tremors of the upper extremities. History of venereal disease years back. Addicted to drink. Well nourished individual. Oedema of the ankles and dorsum of the feet. Tremors of the tongue present. Speech tremulous and hesitating. Fine tremors of the hands and fingers, worse on exertion. Slight paresis of the muscles of the left

side of the face. Pupils unequal, react to light. Sphincters of both bladder and rectum involved. Mental condition: Cerebration slow, speech occasionally incoherent, misses one or two letters of his name in writing. Behaviour queer—apathetic in the day and boisterous at times in the nights. Memory poor. C. S. F.: Protein 35 mgs. per cent, globulin (N. A.) ++, Langes curve 15553200. W. R. ++, Blood W. R. ++ Patient rapidly became demented.

Summary.

- 1. A brief summary of the incidence of neurosyphilis from the Indian medical literature is presented.
- 2. Statistics with regard to the incidence of neurological cases

and of cases of neurosyphilis from the records of the King George Hospital, Vizagapatam, are noted.

3. An analysis of 50 cases of neurosyphilis classifying them under the various types with illustrative cases is given.

Conclusion.

- 1. Neurosyphilis is not so rare in India as it is commonly made out in current medical literature.
- 2. Meningo-vascular syphilis forms the great bulk of the cases of neurosyphilis seen in our clinic.
- 3. Cases of tabes and G. P. I. occur, but they are not so common as in the western countries.

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An Analytical Study of the Fractures seen and treated in the Orthopaedic Department General Hospital, Madras.

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The following cases were seen in 1937-38:—

I. Fractures of scapula:—2.

- (a) Neck Right Side, age 27, male.
- (b) Body—Nil.
- (c) Acromion process—1.
- (1) Right side, 29, male.

with a large amount of callus, but there were no pressure symptoms over the brachial plexus. Two cases of ununited fractures of clavicle were seen, but both of them, young adults, had undergone open operative treatment by wiring elsewhere. As the function was excellent, no further treatment was adopted.

(c) Special sites:

(N.B.—Separate Acromion epiphysis was noticed four times,

- (1) Inner third—2 (one aged 43 another aged 3).

II. Fractures of Clavicle:—127 } Complete 120. } Greenstick 7.

- (a) Right side—69, Left side—57, Bilateral—1.
- (b) Age period.

| Years.       | No. of cases. |
|--------------|---------------|
| 0 to 5       | 42            |
| 5 to 10      | 23            |
| 10 to 20     | 24            |
| 20 to 30     | 18            |
| 30 and above | 20            |

- (2) Junction of inner two-thirds with outer third, 49 out of which 22 were with displacement and 26 without displacements.

- (3) Middle third—50.
- (4) Outer fourth—17.
- (5) Multiple fractures—1.

- (6) Fracture clavicle with separation of epiphysis of acromion—1.

The youngest was 10 days and the oldest 60 years.

- (7) Greenstick variety—8.

- Several cases of old fractures of clavicle were seen, sometimes

The case of multiple fracture was on the left side in a man aged 26. The case of bilateral

fracture was at the junction of the outer and middle thirds in a male child of two years; the fracture at the acromial end was associated with fracture of the third rib at the angle, on the left side, in a man aged 50.

*N.B.*—It is as well to know that a spontaneous fracture of the first rib may occur and a large amount of callus may form producing pressure symptoms on the brachial plexus.

There was one case of a fracture at the junction of the middle and outer third with fracture of acromion process of scapula on the right side in a man aged 22.

### III. Fractures of Humerus—261 cases:—

(a) Anatomical neck—1, age 29, male.

(b) Surgical neck—11.

Left side—7, right side—7.

Impacted—2.

6 males; 5 females.

| Age period. | No. of cases. |
|-------------|---------------|
| 10 to 20    | 2             |
| 20 to 30    | 1             |
| 30 to 40    | 1             |
| 40 to 50    | 1             |
| Above 50    | 6             |

(c) Greater tuberosity.—Nil.

(d) Fracture dislocation head, 1, aged 34, male.

Fractures of the surgical neck are treated by reduction under

anæsthetic by traction and adduction of the arm to the side of chest. The wrist is supported with a cuff and collar, massage to the shoulder and active movements to the elbow and wrist are practised from the beginning. The results have been satisfactory.

The fracture dislocation head was of three months' duration and he came here with pressure over the axillary vein and nerve cords. The head of the humerus was excised. The result was satisfactory when the patient was seen three months after operation.

(e) Fracture of shaft of the humerus, 25.

Upper third—8.  
Middle third—10.  
Lower third—7.

Side: Left side 10 Right side 15  
Males 17 Females 8

| Age period.  | No. of cases |
|--------------|--------------|
| 1 to 5       | 5            |
| 5 to 10      | 5            |
| 10 to 20     | 5            |
| 30 to 30     | 3            |
| 30 to 40     | 3            |
| 60 to 50     | 1            |
| 50 and above | 3            |

One new born baby had musculo-spiral paralysis but recovered satisfactorily. There were two cases of delayed union both in anæmic women. Immobilization from the axilla down to the metacarpo-phalangeal-joint is essential. One case of ununited

fracture with loss of bone and musculo-spiral paralysis of one year's duration came from the mofussil and was treated with a massive inlay bone graft.

(f) (1) Supra-condylar fractures—209.

|       |        |     |
|-------|--------|-----|
| Side: | Left   | 135 |
|       | Right  | 74  |
| Sex:  | Male   | 155 |
|       | Female | 54  |

| Age period. | No. of cases. |
|-------------|---------------|
| 0 to 5      | 52            |
| 5 to 10     | 91            |
| 10 to 20    | 55            |
| Above 20    | 11            |

(one case at 69 years).

(2) Level of the fracture:

|                         |     |
|-------------------------|-----|
| Above olecranon fossa   | 175 |
| Through olecranon fossa | 26  |
| T shaped fractures      | 8   |

|                      |     |
|----------------------|-----|
| Incomplete fractures | 15  |
| Complete fractures   | 194 |

|                      |     |
|----------------------|-----|
| Without displacement | 104 |
| With displacement    | 90  |

The nature of the displacement was forward in one case, lateral in ten cases, medial in five cases, and the rest backward displacements. The elbow joint was involved in seven cases. Fifteen cases came with excess of callus.

(g) Dicondylar: 1 Right side, 1, age 4, male child: 1.

(h) Condyles: 9 External 4, Internal 5 (two involved joints and three did not).

(i) Medial epicondyle 4 (involving joint 1).

Fractures of the lower end of the humerus should be looked upon as important cases of emergency which require adequate attention. They are classified as follows:

1. Supra condylar: i.e., through the broad part of the shaft, a couple of inches above the joint.

2. Infra condylar: Occurs in the flattenedout portions of the bone. The plane of fracture passes from epicondyle to epicondyle with the plane higher on the posterior than on the anterior surface.

3. Dicondylar: Similar transverse plane which crosses the olecranon fossa and is above the epiphyseal line. In this type lateral displacements—outward or inward—is more common than posterior.

4. The lower fragment may be split down towards the joint or a shell may be split off the anterior or the posterior surface. There may be four varieties of injury to the lower fragment:

(a) The lower fragment is split.

(b) Fracture of the condyles.

(c) T. shaped fracture.

(d) Upper fragment pushed down between two lateral ones and in contact with the ulna.

It is necessary to realise that the reduction must be done immediately after the injury, before

the onset of swelling. In cases so treated, there had been no complications and the joint movements have been perfect. When the patient arrives with an enormous swelling or with a history of previous unsuccessful reduction the end result is not quite satisfactory. There is a certain amount of restriction in the elbow joint movements and occasionally there is excess callus formation. The routine adopted is to practise immediate reduction even where there is swelling. An immediate relief in the tension of the part is noticed if the reduction is satisfactory. It is wise not to wait for the swelling to disappear. In the absence of reduction the swelling may not disappear for four or five days. In the presence of swelling the position is kept up by cuff and collar bandage, the patient is brought to the ward, the limb is elevated by pillows still the swelling disappears. In all other cases, after reduction, immobilisation in plaster casing extending from the insertion of the deltoid to the metacarpo-phalangeal joint with the elbow flexed to 40° and the forearm supinated, is done. Immobilisation is kept up for three weeks. No case of Volkmann's ischæmic contracture or myositis-ossificans or injury to the nerves was met with in these cases. All cases of Volkmann's ischæmic contracture that come to the hospital come from outside. It is the practice of the bone setter to massage vigorously these fractures and large numbers of myositis ossificans are met with. Twenty-two cases of myo-

sitis ossificans were seen, 18 males and 4 females.

| Age periods | No. of cases. |
|-------------|---------------|
| 1 to 10     | 4             |
| 10 to 20    | 6             |
| 20 to 30    | 6             |
| 30 to 40    | 6             |

Right side 11, Left side 7, (Site not available for 4) one case a male aged 21 was associated with Volkmann's ischæmic contracture.

In one case, the bony mass was continuous with the head of the radius.

Myositis ossificans is met with in the substance of the brachialis anterior, and in the triceps muscle filling up the olecranon fossa. If the case is of four to six months' duration, excision of these bony blocks is practised but the original movement does not recur; there is always a certain amount of limitation of movement. Prevention is better than cure. If the supra-condylar fracture is not reduced, nerve injuries are more commonly met with. Two cases of unreduced supra-condylar fracture with backward displacement came with musculo-spiral paralysis. In the operation, it was discovered that the lower end of the upper fragment was impinging on the nerve, and the rest of the nerve up to the entrance in the supinator brevis, was one large neuroma. These complications can only be avoided by immediate and proper reduction. There were two cases of cubitus valgus due to fractures. Correction was

obtained by supra-condyloid osteotomy. Anterior transposition of the ulnar nerve was done in one case.

#### IV. Fractures of the forearm :- 612.

- (a) Fracture of both bones, 218
- (b) Fracture of ulna alone, 77
- (c) Fracture of radius alone, 317

- (a) Fracture of both bones, 218:

Males 194

Females 24

| Age period.  | No. of cases. |
|--------------|---------------|
| 0 to 5       | 35            |
| 5 to 10      | 46            |
| 10 to 20     | 101           |
| 20 to 30     | 21            |
| 30 to 40     | 9             |
| 40 to 50     | 3             |
| 50 and above | 3             |

#### Level

|                       |     |    |
|-----------------------|-----|----|
| <i>Upper third</i>    | ... | 40 |
| Ulna at higher level. |     | 3  |
| Both same level       | ... | 32 |
| Ulna at lower level.  |     | 5  |
| <i>Middle third</i>   | ... | 78 |
| Ulna at higher level. |     | 5  |
| Both same level       | ... | 58 |
| Ulna at lower level.  |     | 15 |
| <i>Lower third</i>    | ... | 91 |
| Ulna at higher level. |     | 4  |
| Both at same level    |     | 75 |
| Ulna at lower level.  |     | 12 |

There were nine cases as follows:

|           |     |   |
|-----------|-----|---|
| Bilateral | ... | 1 |
|-----------|-----|---|

Radius upper third and ulna middle third ... 3

Radius upper third and ulna lower third ... 2

Radius middle third and ulna lower third ... 1

Both styloid process ... 1

Ulna in two places (upper and middle thirds, the middle third fracture being of a butterfly nature) with also fracture of the radius-middle third ... 1

Of the 218 fractures, 17 were greenstick, 199 were complete, and 2 were incomplete fractures.

The standard treatment adopted is reduction under anaesthesia with suspension by means of a clove hitch applied to the wrist and traction by the operator's foot applied through a flat band at the level of the middle of the arm. After reduction, immobilisation with the elbow at right angles and the forearm supinated is done by a skin tight plaster of paris from the insertions of the deltoid to the metacarpo-phalangeal joint. The results have been satisfactory. The patient is watched week after week. Softening of the plaster requires a reapplication as otherwise angulation may take place. Backward angulation was met with in four instances and had to be corrected. No case of non-union was met with in these cases. Non-union will be met with only when the elbow is not immobilised. Only one case of open

operation was done to bring about proper alignment of the radius. There were two cases of fracture of the upper-third of ulna with dislocation of the head of the radius forwards. They were reduced. In one instance of the old case, in a boy of ten, there was no restriction of elbow movement and the function was satisfactory. It was left alone.

It is important to realise that a radiograph of the elbow joint is always essential in every case of fracture of the forearm. Because unsuspected small cracks of the head of the radius may be present and they be discovered too late when supination would not be possible.

Three cases of such types were met with.

(b) Fractures of ulna alone, 77.

|                    |              |               |
|--------------------|--------------|---------------|
| Side:              | Right        | 53            |
|                    | Left         | 24            |
| Sex:               | Male         | 64            |
|                    | Female       | 13            |
| Age period.        |              | No. of cases. |
| 0 to 5             | ...          | 9             |
| 5 to 10            | ...          | 8             |
| 10 to 20           | ...          | 15            |
| 20 to 30           | ...          | 16            |
| 30 to 40           | ...          | 22            |
| 40 to 50           | ...          | 5             |
| Above 50           | ...          | 2             |
| Level:—Upper third |              | 27            |
|                    | Middle third | 10            |
|                    | Lower third  | 39            |
|                    | Bilateral    | 1             |
| Upper third:—      |              |               |
|                    | Olecranon    | 10            |
|                    | Coronoid     | 2             |

|             |     |               |
|-------------|-----|---------------|
| Shaft       | ... | 15            |
| Olecranon   | ... | 8 males.      |
|             |     | 2 females.    |
| Age period. |     | No. of cases. |
| 10 to 20    | ... | 1             |
| 20 to 30    | ... | 3             |
| 30 to 40    | ... | 3             |
| 40 to 50    | ... | 3             |

Fracture of coronoid, 1 male and 1 female (aged 25).

All varieties as subperiosteal transverse chipping, and avulsion were met with. It well to realise that an open operation is not necessary if the fragment can be kept in apposition by manipulation; only two cases were operated on. As regards the technique, if holes are bored both in the upper and the lower fragments, the ligature will pull through as the bone trabeculae are longitudinal in direction. The method employed was, to pass the kangaroo tendon through a drill hole through the lower fragment and tie it securely. Another kangaroo tendon is passed through the top part of the olecranon and to bring the two ends which are looped through the lower kangaroo tendon and then tied in position. The results have been satisfactory.

*Middle third:* No difficulty or complication was met with during treatment.

*Lower third:—*

|                 |     |    |
|-----------------|-----|----|
| Styloid process | ... | 8  |
| Shaft           | ... | 31 |

No case of non-union was met with in this series.

|                              |     |
|------------------------------|-----|
| Fractures of radius alone... | 317 |
| Radius upper third           | 71  |
| Radius middle third          | 25  |
| Lower third                  | 221 |

location either at the upper or at the lower end in course of time.

|                          |    |
|--------------------------|----|
| Radius middle third, 25. |    |
| Sex: Female              | 1  |
| Male                     | 24 |

Upper third:—

|           |    |
|-----------|----|
| Sex: Male | 67 |
| Female    | 4  |

|             |     |               |
|-------------|-----|---------------|
| Age period. |     | No. of cases. |
| 0 to 5      | ... | 3             |
| 5 to 10     | ... | 9             |
| 10 to 20    | ... | 33            |
| 20 to 30    | ... | 14            |
| 30 to 40    | ... | 9             |
| 40 to 50    | ... | 2             |
| Above 50    | ... | 1             |

|       |           |    |
|-------|-----------|----|
| Site: | Head      | 20 |
|       | Neck      | 12 |
|       | Shaft     | 38 |
|       | Epiphysis | 1  |

|                     |    |
|---------------------|----|
| Head: Chip fracture | 5  |
| Other fractures     | 15 |
| (with displacement  | 14 |
| without             | 1) |

One case was a T-shaped one involving the joint. One was impacted. One case had fracture of olecranon also, one case had epiphysitis, one was a fracture through the neck with separation of epiphysis. Reduction and immobilisation with elbow at right angles with forearms supinated is the routine treatment. Excision of the head is not satisfactory when the cases are followed up. If the orbicular ligament is intact, however deformed the head is, adaptive changes take place and the functional result is satisfactory. If one of the forearm bones is shortened, there will be a dis-

|               |     |               |
|---------------|-----|---------------|
| Age incidence |     | No. of cases. |
| 0 to 5        | ... | 4             |
| 5 to 10       | ... | 2             |
| 10 to 20      | ... | 2             |
| 20 to 30      | ... | 6             |
| 30 to 40      | ... | 11            |
| 40 to 50      | ... | nil           |

Radius lower third, 221.

|          |        |     |
|----------|--------|-----|
| Sex:     | Male   | 166 |
|          | Female | 55  |
| 0 to 5   | ...    | 2   |
| 5 to 10  | ...    | 8   |
| 10 to 20 | ...    | 49  |
| 20 to 30 | ...    | 44  |
| 30 to 40 | ...    | 35  |
| 40 to 50 | ...    | 40  |
| 50 to 60 | ...    | 26  |
| Above 60 | ...    | 17  |

Level of fracture:

|                                 |     |    |
|---------------------------------|-----|----|
| Up to half an inch              | ... | 62 |
| Half to 3/4 inch                | ... | 27 |
| 3/4 to one inch                 | ... | 47 |
| One to 1-1/2 inch               | ... | 11 |
| Two inches and above            | ... | 64 |
| Styloid process of radius alone | ... | 10 |

Fracture with displacement 58 out of 221.

Fracture with involvement of joint, i.e., fracture involving the articular surface generally, vertically. 20 out of 221.

Fracture with styloid process of ulna ... 69 out of 221

The statement made here that the fracture of the lower third of the radius is enormously common in males is due to the fact that a large number of males between 10 and 40 get occupational injuries as those resulting from cranking a car or fall from a bicycle. If the fragments are displaced, then the problem is not different from a Coles's fracture occurring in an elderly person. They are reduced under an anæsthetic, generally by Robert Jones's method and immobilized from below the elbow to the metacarpo-phalangeal joint in plaster for four weeks. Active movements of fingers, elbow and shoulders are encouraged from the beginning. Particular care must be taken to enquire about shoulder pains, especially in patients above thirty-five. There are occasions in which Thomas' wrench is required to reduce the fracture. In old unreduced cases of Coles's reduction is attempted under a general anæsthetic, provided, the general condition is satisfactory and the arteries are not calcareous.

No case of involvement of median nerve was noted. One case of rupture of extensor pollicis tendon was noticed.

#### V. Fractures of Carpal Bones :

There were three cases of fracture navicular: all of them males aged 18, 20 and 25, one case was an ununited fracture and two cases of transverse fracture. There was one case of osteochondritis of carpal bones after a trivial injury in a man of 18.

#### VI. Fractures of Metacarpal Bones : Total 75.

|                      |    |
|----------------------|----|
| First Metacarpal ... | 13 |
| Second Metacarpal... | 23 |
| Third Metacarpal ... | 5  |
| Fourth Metacarpal.   | 17 |
| Fifth Metacarpal ... | 17 |
| Multiple ...         | 7  |

Sides : Right side, 49  
Left side, 26

Sex : Male, 70  
Female, 7

| Age period.  | No. of cases. |
|--------------|---------------|
| 0 to 5 ...   | <i>Nil.</i>   |
| 5 to 10 ...  | <i>Nil.</i>   |
| 10 to 20 ... | 12            |
| 20 to 30 ... | 42            |
| 30 to 40 ... | 9             |
| 40 to 50 ... | 11            |

Site : Base, 7  
Shaft, 53  
Neck and head, 6  
Bennet's Fracture, 9  
Base involving joint, 1  
Not involving joint, 5  
Chip fracture, 1

Shaft—with displacement, 11 }  
No displacement, 42 } 53

Bennet's fracture :

Age period 20—30 except one case aged 37.

Neck and head :

Involving joint ... 0  
Not involving joint ... 6

Fractures of metacarpals are treated with plaster casing extending from the elbow to just below the metacarpo-phalangeal

joint. Angulation must be corrected. If there is marked displacement, a wire is incorporated in the plaster, a rectangle extending four inches below the phalanges. Finger extension is obtained either from the nail or by skin traction applied to the finger. If there is backward angulation, it will interfere with the mobility of the metacarpo-phalangeal joint. Old untreated cases are seen with forward displacement of the head and deviation of axis of the fingers. They lead to loss of efficiency.

#### VII. Fracture Phalanges : 74.

Sex : Male ... 64  
Female ... 10

| Age period.      | No. of cases. |
|------------------|---------------|
| 0 to 5 ...       | <i>Nil.</i>   |
| 5 to 10 ...      | 1             |
| 10 to 20 ...     | 25            |
| 20 to 30 ...     | 20            |
| 30 to 40 ...     | 18            |
| Above 40 ...     | 10            |
| Side : Left ...  | 36            |
| Right ...        | 38            |
| First phalanx 50 | 69            |
| Second 9         |               |
| Terminal 10      |               |
| Multiple 5       |               |

Site: (a) Base.—Involving joint 9  
Not involving joint 7

16

(b) Shaft:—With displacement 12

Without displacement 46

58

|            |    |
|------------|----|
| Impacted   | 2  |
| Comminuted | 14 |
| Transverse | 27 |
| Vertical   | 3  |

46

(c) Head, 7. This totals up to 81 including multiple fractures.

Fracture of phalanges are treated with extension when there is displacement; if there is no displacement on a bent aluminium splint after reduction.

#### VIII. Fracture Spine : 7

Sex : Male, 6  
Female, 1

Compression fracture of lumbar vertebræ 5, dorsal vertebra 1.

One case was a fracture of the transverse process male aged 42 of the secured lumbar vertebra. There was one case of fracture of the coccyx.

| Age period.  | No. of cases. |
|--------------|---------------|
| 1 to 10 ...  | <i>Nil.</i>   |
| 10 to 20 ... | 1             |
| 20 to 30 ... | 2             |
| 30 to 40 ... | 2             |
| Above 40 ..  | 2             |

This number does not represent the number of cases treated in this hospital. There is no means of diagnosing a compression fracture of spine excepting by looking for it and X-raying all cases who complain of pain in the back and all cases who have had a fall from a height. An elderly lady slipped and fell in the bath room,

the cause of her pain went unnoticed in several hospitals while an X-ray here showed compression fracture of the first lumbar vertebra a fall from a cycle can cause it.

They are all treated in a hyper-extension plaster and we have seen that the vertebra very often recovers its original shape. The plaster must be kept on for four months. It must extend from the supra sternal notch to the symphysis pubis. The patient must be made to exercise his limbs. During the first two or three days of hyperextension, abdominal distension is often met with and is treated with pitressin injections. There are many cases met with, where callus formation is seen in these cases, on the anterior aspect of the body of the vertebra. They often complain of back pains and a follow up shows that these men require reeducative exercises of the muscles of the back. The cases with paraplegia do not get on well, as many of them had developed bed sore and cystitis. Although these men do not return to their former occupations, they need not be economically useless. There is at the moment a foreigner, who had a compression fracture of the twelfth dorsal vertebra eight years ago. He has incontinence of urine and faeces and a perforating ulcer of the foot. For the incontinence of urine he is fitted up with a rubber urinal to his penis and he is an earning member still.

There was one case of cauda-equina injury.

#### IX. Fracture of pelvis:

There were two cases of multiple fracture of the rami without complications.

#### X. Fractures of the Femur.

|             |     |    |
|-------------|-----|----|
| Upper end   | ... | 51 |
| Shaft       | ... | 22 |
| Lower third | ... | 4  |

Upper end: Sex: Males, 86  
Females, 15

| Age period. | No. of cases. |
|-------------|---------------|
| 1 to 10     | 1             |
| 10 to 20    | 5             |
| 20 to 30    | 2             |
| 30 to 40    | 6             |
| 40 to 50    | 5             |
| Above 50    | 32            |

Site: Pertrochanteric fracture: 17

Age 40 to 60

Sub-capital 7

3 below forty and 4 above forty years.

Subtrochanteric, 13.

Pathological fracture, 2.

Malunited fracture of neck, 2

Fractures through the root of the greater trochanter, 5.

Fractures through the greater trochanter, 5.

Fractures through the broadest part of neck, 2

Comminuted fractures, 2.

Three of these cases ended in malunion and two had excessive callus.

It will be seen from this, that sub-capital fracture is only 7 and the rest occur in either the broad part of the neck or in the trochanteric area. Consequently a great majority of these cases can be treated with confidence and will give a satisfactory bony union.

Sub-capital fractures carry a certain percentage of mortality in old people on account of the conditions present in old age.

Sub-capital fractures are treated by one of the following two methods:

(a) After reduction under an anaesthetic, they are put in plaster casing. Reduction is effected by traction and is followed up by 45° abduction, 15° internal rotation, extension at the hip and flexion at the knee. A Hawley's table helps but this can be managed on any two tables. The plaster casing extends from the level of the nipple to the toes with immobilisation of the opposite hip leaving the opposite knee joint free. This must be kept on for four months, weight bearing being permitted after the third month with the plaster on. Bony union results and the working capacity of the individual, including car driving is very satisfactory. One case of sub-capital tape was met with in a boy of fourteen. He had hypopituitary syndrome. (b) The second method of treatment is by the insertion of a Smith Peterson's pin. This involves an X-ray plant, with screen examination facilities.

Only 3 special instruments are required which do not cost much. My practical experience in this is limited to five cases but reports from other workers are encouraging. Fractures in the region of the trochanter are treated by traction after reduction under an anaesthetic. The traction may be skin traction or skeletal traction by a pin. The angular deformity must be properly corrected.

Fracture of the shaft:

|              |     |    |
|--------------|-----|----|
| Upper third  | ... | 9  |
| Middle third | ... | 13 |

Males 10; Females 3.

| Age period | No. of cases. |
|------------|---------------|
| 1 to 10    | 6             |
| 10 to 20   | 2             |
| Above 20   | 5             |

One case was comminuted. There was anterior angulation in two and a lateral angulation in one.

Fractures of the shaft of the femur are treated by pin-traction, by a Kirschner's wire, driven above the condyles. A Thomas' knee splint with a Pearson's knee attachment is used. Accurate apposition and alignment is obtained and the end results are satisfactory. Mobility of the knee is ensured. The pin is removed at the end of three to four weeks, and skin traction is kept up for two to three months. Weight bearing is permitted with plaster casing on, at the end of third or fourth month according to circumstances. There has been

no case of malunion. There was no indication for open operation.

Lower third of Femur ... 4

Sex : Male 3.

Female 1.

Age : 2, 10, 35 and 48.

Involving the condyles, ... 2

Separation of epiphysis ... 2

The two cases of epiphyseal separations are not recent injuries; one of the cases, a boy aged about twelve came with immobility of knee joint. There was no history of injury. There was a swelling on the anterior aspect of the lower end of the femur which simulated a growth. Radiographic appearances showed areas of rarefaction and displacement of the epiphysis forwards, which is the usual displacement. Unless one examines carefully, it is quite possible to overlook a displaced epiphysis. I know of a case where the displacement took place unnoticed during the course of manipulating a flexed knee joint in a boy of ten. Tubercle, sepsis, syphilis, suppuration are the common causes of separation of epiphysis. No causative factor could be found out in these cases. No treatment was adopted as the patient was not willing.

A case of fracture of internal condyle who was treated in 1936 July was followed up. The results are satisfactory in every way. The case was treated by reduction and immobilization without open operation.

There was no complication of gangrene in the lower third end fracture.

#### XI. Fractures of the Patella : 8.

| Age period.  | No. of cases. |
|--------------|---------------|
| 1 to 10 ...  | Nil.          |
| 10 to 20 ... | 3             |
| 20 to 30 ... | Nil.          |
| 30 to 40 ... | 2             |
| 40 to 50 ... | 2             |
| Above 50 ... | 1             |

|                  |   |
|------------------|---|
| Sex: Females ... | 4 |
| Males ...        | 4 |

#### Varieties

|                           |   |
|---------------------------|---|
| Transverse ...            | 4 |
| Incomplete transverse ... | 2 |
| Fissured ...              | 2 |

Four of the incomplete fracture of patella-treated elsewhere were observed and came here for pain in the knee and slight limitation in flexion. They were treated with manipulation of the knee. My former practice was to treat transverse fracture of patella by open operation, bringing the two ends together with Kangaroo tendon passed through drill holes through both fragments. On two occasions, I used silk ligature but it was not satisfactory. Fifteen years ago, silver wire was used and two or three of my cases gave trouble and the wire had to be removed. It is important to secure accurate alignment of both the fragments; otherwise osteo arthritis results. It is not always possible to follow up one's own cases but the following case

gives a fair idea of the convalescent period taken by the patient:—A strong healthy man of thirty years was operated in June 1937 by me for transverse fracture of patella, using kangaroo tendon. The limb rested in a Thomas's splint for two weeks and from the third week, the patient began to move his knee. Being an educated man, he co-operated in massaging the quadriceps from the beginning. He was discharged from the hospital in the sixth week for clerical work, but he was undergoing Faradization for four months. At the end of six months, there was still limitation of flexion by 10°, and there was some wasting of quadriceps muscle. Consequently, I have resorted to excision of patella now. In the last four cases, two females and two males excision of the patella was done. This is not a new method of treatment. In former days, in comminuted open fractures the whole patella was removed (Speed). Quenn and Gatellier mention Chaput's subperiosteal resection of the upper fragment. In old fractures of patella, if it was not possible to approximate the bone fragments, excision of the bone can be performed (Speed).

It should be remembered that the blood supply to the patella is poor and the bone is extremely friable. I know of an instance where the whole bone necrosed after an open operation in a woman of twenty-five. After excision of the patella, no splinting is used. The patient is able

to move the knee from the third or the fourth day, full range of movements being obtained by the end of a fortnight. There is slight difficulty in completing the extension in the sitting position. Excision of the patella is a notable improvement, in a fracture of this type.

#### XII. Fractures of the Leg : 106.

|                  |    |
|------------------|----|
| Tibia alone ...  | 39 |
| Fibula alone ... | 11 |
| Both ...         | 56 |

(a) Tibia alone ... 39

Sex : Males, 26.  
Females, 13.

|                            |      |
|----------------------------|------|
| Upper third of the bone. 4 | } 39 |
| Middle third ... 11        |      |
| Lower third ... 19         |      |
| Medial malleolus ... 5     |      |

#### Transverse fractures :

|                  |      |
|------------------|------|
| Upper third ...  | Nil. |
| Middle third ... | 3    |
| Lower third ...  | 4    |

#### Oblique fractures :

|                  |   |
|------------------|---|
| Upper third ...  | 3 |
| Middle third ... | 4 |
| Lower third ...  | 9 |

#### Comminuted fractures :

|                  |     |
|------------------|-----|
| Upper third ...  | Nil |
| Middle third ... | 1   |
| Lower third ...  | 1   |

#### Vertical crack :

|                  |   |
|------------------|---|
| Upper third ...  | 1 |
| Middle third ... | 2 |
| Lower third ...  | 2 |

#### Spiral :

|                  |     |
|------------------|-----|
| Upper third ...  | Nil |
| Middle third ... | 1   |
| Lower third ...  | 3   |

| Age period | Upper third | Middle third | Lower third |
|------------|-------------|--------------|-------------|
| 1 to 10    | Nil         | 6            | 9           |
| 10 to 20   | Nil         | 3            | Nil         |
| 20 to 30   | 1           | 2            | Nil         |
| 30 to 40   | 2           | Nil          | 10          |
| 40 to 50   | 1           | Nil          | cases       |
| Above 50   | Nil         | Nil          |             |

Fractures of the fibula alone, 11.

Sex: Males, 7.

Females, 4.

|                  | Trans-verse | Oblique | Spiral | Comminuted |
|------------------|-------------|---------|--------|------------|
| Upper third ...  | Nil         | Nil     | Nil    | Nil        |
| Middle third ... | Nil         | Nil     | Nil    | Nil        |
| Lower third ...  | 2           | 3       | 1      | 1          |

Fibular Malleolus, 4.

| Age period. | Lower third. | Fibular malleolus. |
|-------------|--------------|--------------------|
| 1 to 10     | — Nil        | Nil                |
| 10 to 20    | — 2          | Nil                |
| 20 to 30    | — 3          | 2                  |
| 30 to 40    | — 1          | 1                  |
| 40 to 50    | — 1          | 1                  |
| Above 50    | — Nil        | Nil                |

Fractures of both bone of leg 56.

Sex: Males, 42.

Females, 14.

| Level.           | Oblique. | Trans-verse. | Comminuted. | Spiral. |
|------------------|----------|--------------|-------------|---------|
| Upper third ...  | Nil      | 3            | Nil         | Nil     |
| Middle third ... | 3        | 2            | 3           | 9       |
| Lower third ...  | 12       | Nil          | 12          | 3       |

Both malleoli, 6.

Shaft of tibia with fibular malleolus, 2.

Shaft of fibula with medial malleolus, 2.

Abduction fracture at the ankle joint, 6.

Of the 27 lower third fractures in seven cases the fibula was fractured at a higher level and tibia in five cases. The rest were at the same level.

| Age period. | Upper third.  | Middle third. | Lower third. |
|-------------|---------------|---------------|--------------|
| 1 to 10     | 1             | 2             | 16           |
| 10 to 20    | Nil           | 3             | 5            |
| 20 to 30    | 1             | 2             | 8            |
| 30 to 40    | Nil           | 1             | 8            |
| 40 to 50    |               |               |              |
| Above 50    | Rest 9 cases. |               |              |

Most cases of fractures of the leg are managed as out-patients after reduction, for which they are admitted into the hospital for two or three days. No elaborate apparatus is required. The patient is anaesthetised, vertical traction is applied through a clove hitch at the ankle, the knee flexed at the end of the table the thigh resting on a sand bag. Most fractures can be manipulated in this position, but some cases do not require flexion at the knee. This can only be judged during the manipulation. A skin tight plaster is applied from the toes to the middle third of the thighs with the knee in the position which has given the most satisfactory apposition. Care is taken to see that there is no deviation of the foot medially or laterally. The inner border of the patella, the medial malleolus and the inner border of the great toe must be in alignment. The foot is generally kept at right angle but a slight equinus position is

required in lower third fractures. Every case has resulted in union. Only one case required open operation in a boy of twelve to remove the interposed tibialis anterior. The plaster casing is kept on for twelve weeks on the average. The casing is inspected every fortnight. Backward and lateral angulation must be watched during the period. One case developed backward angulation. Another had lateral angulation.

They were corrected on a wedge. Common peroneal nerve paralysis must be looked for in upper third injuries. One case of fracture of upper ends of both bones in a man aged 31 had impaction of fragments into the articular surfaces. There was one case of separation of lower epiphysis of tibia in a male aged 13. A male aged 23 had fracture of bones, upper third, at the same level, and this was followed by new bone formation of the interosseous membrane. He was not a native of Nellore District. The new bone formation was not due to flourine poisoning. One case of lower third fracture in a man aged 50 had symptoms of calcaneus spur. A man aged 40 with fracture of both bones of the leg had calcareous popliteal artery. But there was no complication.

### XIII. Fractures of the Tarsus. 25

|                 |        |
|-----------------|--------|
| Calcaneus       | ... 14 |
| Talus           | ... 5  |
| Cuboid          | ... 3  |
| First cuneiform | ... 2  |
| Navicular       | ... 1  |

Fractures of Calcaneus, 14.  
Sex: Males, 12, Females; 2.

| Age period.                    | No. of cases. |
|--------------------------------|---------------|
| 1 to 10                        | ... 3         |
| 10 to 20                       | ... 6         |
| 20 to 30                       | ... 3         |
| 30 to 40                       | ... 1         |
| Above 40                       | ... 1         |
| Crushed fractures.             | 4             |
| Longitudinal crack incomplete. | 2             |

Fractures of the body. 8

No fracture of avulsion type was met with.

It is true that most of the fractures occur in the third and fourth decade, but they have been found in children as well as in the aged as late as 70. In all instances except one, it is invariably the result of a fall from a height upon the feet. In one instance of a boy of 12, the inferior surface of the calcaneus had a longitudinal fracture completely separating the inferior articular surface. These fractures can invariably be diagnosed clinically by the following signs.

- (1) Swelling of the heel.
- (2) By the bulge on the external malleolus.
- (3) By the tenderness on pressure over the heel.
- (4) Movements of the ankle are free.
- (5) Movements of the foot in the lateral plane at the

subastragaloid joint are extremely painful and greatly restricted.

Two cases were met with, associated with compression fracture of spine.

There is a large divergence of opinion as to the methods of treatment of compression fractures. One school leaves the fractures unreduced but immobilized. The other school tries to restore the original shape of the calcaneus by various methods. These various methods are reduction under anaesthetic with the help of (a) Bohler Redresseur, (b) pin-traction, and (c) with a wrench. All these methods have been adopted by me but on account of the difficulty of a follow up, one cannot easily lay down rules.

A male doctor aged about 28 was treated for his compression fracture of the calcaneus by reduction with Bohler's redresseur and immobilization in plaster in 1933 October. He has been radiographed periodically. His subastragaloid joint is free and he is doing active work. On the other hand, a bilateral compression fracture in a man aged 50, who was also a diabetic in 1935 has resulted in painful feet. His walking capacity is limited to about a furlong at a time. Such patients may be benefited sometimes by manipulation of the foot or by an arthrodesis of the foot. Untreated cases of all ages come after six months to a year for painful feet. One young man

aged about 20 had a compression fracture of the spine and a compression fracture of os calcis one year ago. His foot is very painful and therefore an arthrodesis has been done. So, in my opinion, all these cases must be treated and an attempt made to secure proper reduction.

The causes of disability are:

(1) Traumatic flat foot. This is the result of uncorrected upward displacement of the posterior portion of the os calcis. (2) Lateral displacement of the heel is not corrected and hence weight is transmitted to the medial side of the posterior pillar of the arch. Hence a pronated foot results. (3) Limitation of the lateral movements of the foot. The lateral movements of the foot serve an important purpose in allowing the foot to conform to the irregularities of the ground. (4) Spur formation on the under surface of the os calcis. We must avoid the many causes of disability by treating the fracture. Hence every case must be reduced under an anaesthetic and put up in plaster. Weight bearing must be allowed only after eight weeks. But active movements of the toes must be encouraged from the beginning. It has been observed by me that a pin traction alone does not bring about a restoration of the form of the os calcis. Some cases are associated with fracture of talus generally, chip fracture. One case showed areas of rarefaction and spur formation on talus. Another had an accompanying fracture of the Navicular.

### An Analytical Study of the Fractures

Fractures of Talus: 5

Males, 43.  
Females, 2

| All males.  |               | Age period |     | No. of cases. |
|-------------|---------------|------------|-----|---------------|
| Age period. | No. of cases. |            |     |               |
| 1 to 10     | Nil           | 1 to 10    | ... | 2             |
| 10 to 20    | 2             | 10 to 20   | ... | 12            |
| 20 to 30    | 3             | 20 to 30   | ... | 14            |
|             |               | 30 to 40   | ... | 10            |
|             |               | Above 40   | ... | 7             |

One case was a comminuted fracture involving the body and the trochlear surface in the right side in a man aged about 30. One was a crushed fracture of the talus with chipping of the anterior margin of the tibia, with backward displacement of the talus in a male aged 30. One was a fracture of the neck of the talus in a male aged 30.

Five were transverse and five were comminuted of these.

They are treated with a plaster boot extending up to the tubercle of the tibia. Untreated cases develop a troublesome oedema which takes long time to disappear. Most young patients return to work, at the fourth week, but older patients require massage and active movements before they return to work. They complain of a stiff painful foot which requires manipulation after two months.

Fractures of the Cuboid: 3

All males. Age: 25 to 40.  
First cuneiform, 2.  
Both males 30 years old.

One case of fracture of navicular in a man aged 45 was associated with fracture of calcaneus.

### XV. Fracture of Phalanges:

Total 35: Right foot ... 23  
Left ... 12

Males, 28; Females, 7.

### XIV. Fracture of the Metatarsals

| First meta-tarsal. | Base of 1, 2, 3 | Base, Shaft, Head |       |      |
|--------------------|-----------------|-------------------|-------|------|
|                    |                 | Base              | Shaft | Head |
| First meta-tarsal. | 2               | Nil               | Nil   | Nil  |
| Second alone       | 3               | 4                 | 1     | 1    |
| Third              | 1               | 1                 | Nil   | 1    |
| Fourth             | 2               | Nil               | 1     | 1    |
| Fifth              | 15              | 8                 | 1     | 1    |

Fractures involving more than one meta-tarsals were 8. First, second and third 3, second and third 1, second, third and fourth 1, third and fourth 1, fourth and fifth 2.

|            | First Phalanx. | Second Phalanx. | Third Phalanx. |
|------------|----------------|-----------------|----------------|
| Great toe  | 12             | 7               | Nil            |
| Second toe | 7              | 2               | Nil            |
| Third toe  | 2              | Nil             | Nil            |
| Fourth toe | Nil            | Nil             | Nil            |
| Fifth toe  | 2              | Nil             | Nil            |

There were two cases of fractures of more than one phalanx. Fracture separation of epiphysis of proximal phalanx of middle toe was only one.

| Age period. | Number of cases |
|-------------|-----------------|
| 1 to 10     | Nil             |
| 10 to 20    | 6               |
| 20 to 30    | 8               |
| 30 to 40    | 7               |
| Above 40    | 14              |

|                                                 |    |
|-------------------------------------------------|----|
| Total number of cases with lateral displacement | 2  |
| Comminuted fractures                            | 10 |
| Fractures involving the articular surface       | 3  |

Treatment of fractures of phalanges are carried out on the same principle as fractures of phalanges of upper extremities. A troublesome arthritis of interphalangeal joints is an occasional unexpected complication met with more in the upper extremity than in the lower extremities even though the articular surface is involved. So the finger joints must be kept in suitable position from the commencement of the treatment, so as not to interfere with the occupational efficiency of the individual.

XVI. Fracture of the Nasal Bone, 8.

| Male, 7; Female, 1. |               |
|---------------------|---------------|
| Age period.         | No. of cases. |
| 1 to 10             | 1             |
| 10 to 20            | 3             |
| 20 to 30            | 4             |

These fractures are elevated with a special elevator under a local anæsthetic.

XVII. Fractures of the Mandible: 3.

All males.  
Age:—12, 25 and 30.  
One had an impacted wisdom tooth. These cases are treated by Ivy's method. Ivy's method consists in passing a bronze wire number 22 through the intra-dental space on either side of the fracture of the affected jaw, wires are passed in the opposite jaw, exactly opposite. These wires are tightened after the fractures are reduced when satisfactory apposition is obtained. Wires are passed through the upper and lower jaw on either side and twisted together so that the patient cannot open his mouth. The patient is fed through a rubber catheter passed behind the last molar tooth. The mouth is kept sweet by irrigation with 1 in 200 lotio acid carbolio.

XVIII. Fracture of the Zygomatic arch

There were two cases of depressed fracture of the Zygomatic arch, one in a male and the other in a female. The depressed fragments were brought into position by passing an elevator through a small incision below the level of the zygomatic arch. The result is satisfactory.

XIX. Fracture of the Sternum.

There was only one case of fracture of the body of the sternum in a male aged 36. There was no fracture of of the vertebra. The patient gave me an anxious time for a week as he had slight hæmoptysis and a

highly increased pulse rate, the cause of which was not obvious. However he got on well. It is possible for infection of the anterior mediastinum to occur in fracture of the body of the sternum, as was noticed in a case in 1935 during post-mortem examination. I am indebted to Drs. S. V. Tiruvenkatachari, M.B.B.S., and A. S. Annamalai, M.B.B.S., House Surgeons for their co-operation and help, and to the Superintendent of the Hospital for permission to publish these notes.

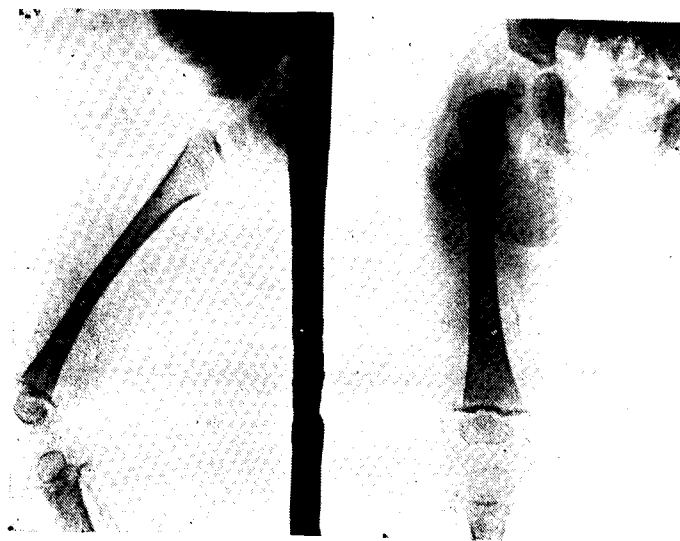
IF

As construed by E. J. B. of Iowa

If she calls you to her bedroom, in the wee hours of the night,  
And through her half closed eyelids you detect a tell tale light;  
If her bosom heaves tumultuously, like the tide upon the ocean  
And her voice is soft and tremulous, betraying her emotion;  
If her nostrils dilate widely with each panting, labored breath  
And her shapely body trembles as might one approaching death.  
If she beseeches and implores you, as she grasps your trembling hand  
To alleviate her suffering, the torture of the damned;  
That's ASTHMA!



I. Annamalai—aged 20.  
Protrusio acetabulum Right.



II. A case of infantile Scurvy. Baby 10 months. Most characteristic lesions are seen at the epiphyseal line. The normal narrow line of ossification is broadened. Fragments of bone are scattered about. There is no cupping of the diaphysis. No periostitis of shaft.

## Clinical Memoranda.

### CLINICAL CASES FROM THE ORTHOPÆDIC DEPARTMENT GENERAL HOSPITAL, MADRAS.

BY N. S. NARASIMHAN, F.R.C.S. (ENG. and IRE).

The following cases are rare cases. Cases of *Protrusio acetabuli* have not been recorded in this hospital before.

I am indebted to the Barnard Institute of Radiology for the X-ray prints and to Dr. N. Ramanathan, M.B.B.S., House Surgeon, for his co-operation and assistance and the Superintendent, General Hospital, for permission to publish these notes.

I. *Protrusio Acetabuli* is a condition first described by Otto in 1824 and is known now after his name as Ottopelvis. The modern terminology of the condition is arthrokatachysis. It is a non-traumatic progressive arthritis of the hip joints. The X-ray appearances are characteristic. The floor of the acetabulum is ballooned in and the head of the femur is completely within the acetabular cavity. The joint space is thinner than usual. The head of the femur is normal in shape and density.

The condition is due to a local softening of the bone with continuous weight bearing and is an error of growth. More than that cannot be said about the ætiology. It may be simulated to a minor degree by osteoarthritis of the hip.

The disease is usually bilateral and is common in females. It is discovered clinically in middle

life although probably in every case it dates from childhood.

The symptoms are stiffening of the hips and pain. These symptoms draw attention usually about the period of adolescence, and hence about the time of onset of menstruation. The loss of movement at the hip joints gets progressively greater.

The following are the reports of two cases of Ottopelvis that have been met with :—

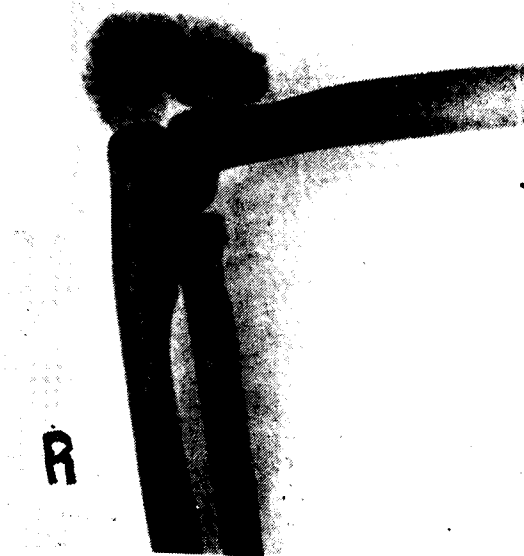
1. Annamalai, age 20, was admitted on 8th April 1938 for a flexor contraction of the right hip. He had no injury and was quite well 6 months ago. The trouble started as swelling of the hip followed by fever and contracture at the hip. There was a spasm of the adductors and the knee was kept in a flexed condition at right angles to the body. The X-ray picture gave the appearance of osteoarthritic



IV. Old dislocation of the Right wrist joint.



V. Malunited fracture of the left femur with Volkmann's Contracture and shortening with the limb externally rotated and adducted.



VI. A case of giant cell tumour under the Right Triceps in a man aged 18 years.



VII. Pelyvis of a case of osteomalacia in a Madras Muhamadan woman aged 25.



VIII. Male Paravertebral abscess (Tuberculous disease of spine)  
Costo-transversectomy Right Side.

changes at the hip and the knee as well. Soutar's fasciotomy was performed and the limb brought to normal level. After a time he was discharged. On 2nd July 1938 he came again and was readmitted for flexor contracture of the same hip. This time the radiograph (No. I) showed that on the right side the head of the femur was smaller and there was a deepening of the acetabulum with projection of the floor into the pelvic cavity. Mantoux's test was negative and there were no visible signs of tuberculosis in other parts of the body.

2. The second case is that of a boy now 12 years of age. It is a case of tubercle of the left hip under observation for the past six years, now healed and the radiograph shows a protrusion of the acetabulum into the pelvic cavity.

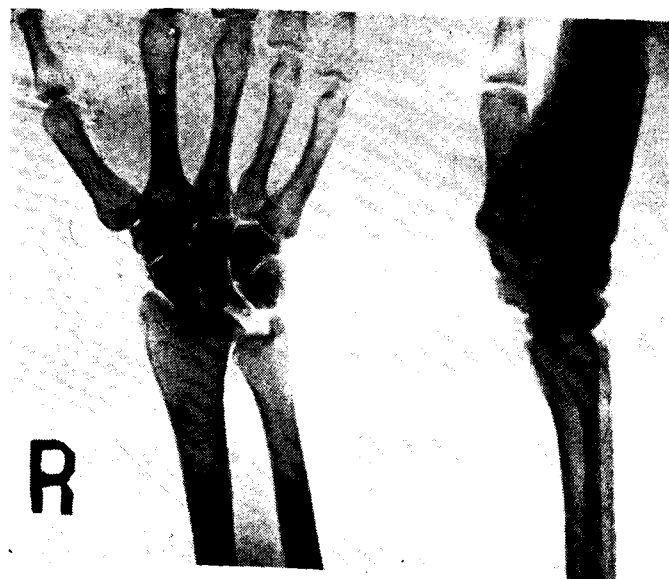
Contrary to the literature of Ottopelvis, the above two cases are both males and the disease has been unilateral. One of them is a case of tuberculosis, whereas the ætiology of the other one is obscure. Does protrusio acetabuli occur in healed cases of tubercle of the hip joint?

II. *A case of infantile scurvy.*—Cases of infantile scurvy are very rare—most students and house surgeons whom I have enquired have not seen any case. In February 1929, I met with a case of subperiosteal hæmorrhage in a male child a year old; the child had melæna but no bleeding gums. I diagnosed it as scurvy

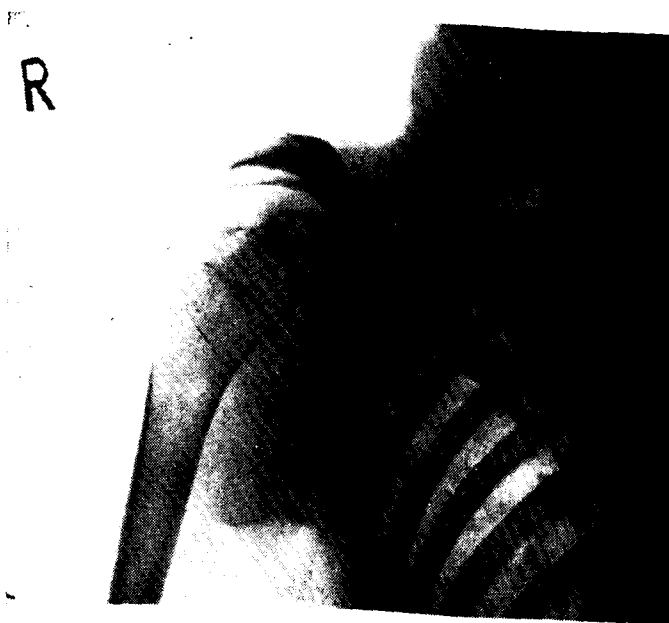
and treated it with fresh lemon juice and oranges; in a week's time the baby improved and his health is quite good now.

Another case was seen with a large swelling of the left thigh, of three weeks' duration, on a baby of ten months, of very well-to-do parents. The child was sent to me as periostitis. There was bleeding from the gums and the child was very difficult to handle. The baby was an artificially fed one. A clinical diagnosis of scurvy was made but the temperature was 103° to 104° and the baby was very ill. The question of acute osteomyelitis was constantly in mind.

A wet film was taken; and the accompanying radiograph No. II shows the characteristic changes. The epiphyseal line is broad; there is bony deposit away from the bone in the muscle; the epiphyseal change is visible in both femur and tibia. (In congenital syphilis there is cupping of the diaphysis, and periostitis of the shaft distinctly to be seen.) The limb was splinted; and treatment ordered for scurvy. On the 3rd and 4th day of the treatment the child looked ill and consequently a small diagnostic incision was made under local anæsthesia; only blood clots were evacuated; the small  $\frac{1}{2}$  inch incision was sutured and the limb splinted. On the 6th day the temperature became normal. The child had an uneventful recovery.



IX. Osteoporosis of the Carpal bones. Right side.



X. Srinivasan—18 years  
Arthrodesis of the Right shoulder for tubercle—4 months  
after the operation.

The case has to be differentiated from acute osteomyelitis; high temperature in subperiosteal hæmorrhages is mentioned by Boyd, Ramanis and Mitchener, although Hutchison in his Diseases of children does not lay stress on this point.

It is interesting to note what is said in Holt's Diseases of children: "Many cases of scurvy come into the hands of the orthopædic surgeon with a diagnosis of joint or spinal disease. Where the swelling was mainly of one limb I have twice known a diagnosis of malignant disease to be made, from the cachexia, the shape of the swelling, the discolouration and the pain. I have known two cases to be operated on by eminent surgeons, once with a diagnosis of sarcoma and one of osteitis of both tibiæ. Not until the subperiosteal hæmorrhages and epiphyseal separation were discovered was the nature of the trouble suspected."

III. *A case of paravertebral abscess and costo-transversectomy.*—In a recent examination of 41 cases of tuberculosis of spine—25 recent cases and 16 old films of past years—it was found that the dorsal vertebræ were the seat of disease in 19 cases. Three cases showed paravertebral abscess in the mediastinum.

A young male of 24 showed disease of the dorsal vertebræ, 9, 8, 7 and 6, without affection of intervertebral disc; the temperature was high ranging from 100°

to 102°; the duration of the disease was one year; there were calcified shadows in the anterior mediastinum also. The pulse rate was steadily high.

In view of the increased pulse rate, the steady high temperature even after two months of immobilisation in plaster and on account of the brisk knee jerks, dysphagia and vomiting, it was thought advisable to do a costo-transversectomy. In *Burgard's System of Operative Surgery* (Vol. II, p. 44), Stiles writes: "If the abscess enlarges, the tension may become so great that the œsophagus, the trachea, and the left recurrent laryngeal nerve may be pressed upon or paraplegia may result from the pus finding its way into the spinal canal. If the above complications occur in spite of efficient rest treatment, operation becomes imperative."

It is advisable to follow Stiles' technique.

The operation was performed under local anaesthesia and a costo-transversectomy of the 8th rib was done on the right side. There was an enormous discharge of pus. The pus was contaminated with streptococci. Tubercle bacilli were found in large numbers on smear examination. Patient felt immediate relief. He developed pleural effusion on right side which was twice aspirated and on both occasions the aspirated fluid was sterile. The patient died a fort-

night after operation. The results of costo-transversectomy are good as, out of the 24 cases collected by Menard, 19 recovered; but Robert Jones remarks that the mortality rate is high after costo-transversectomy. I think the operation must not be unduly delayed.

IV. *Unreduced dislocation of the right radio-carpal joint.*—Anthony, aged 50, was seen on 8th December 1937 while accompanying his son for a fracture. He had an unreduced dislocation of the right radio-carpal joint of 30 years' duration. The function was excellent and he was doing a gardener's job.

The accompanying clinical photo (No. IV) shows the condition. There were no osteoarthritic changes in the wrist joint.

V. *A case of malunited compound fracture of the upper third of left femur.*—Patient, a male, was a discharged railway servant, aged 50. The clinical photo (No. V) shows the malunion of the upper third of the femur after a compound fracture treated elsewhere, and he had a Volkman's ischæmic contracture of all the muscles of the left lower limb. After immunisation with the anti-tetanic and antigas gangrene serum, an osteotomy was done and skeletal traction with Kirschner's wire was adopted. Not much appreciable length was obtained and the patient could not stand the skeletal traction.

A disarticulation at the hip was done by the posterior flap

method after tying the external iliac artery.

The indications for disarticulation were (1) the considerable amount of shortening which could not be overcome by an osteotomy and wire traction, (2) the presence of Volkman's contracture and the uselessness of the limb, and (3) the desirability of getting the patient out of bed as the patient had been in bed for over eighteen months.

Volkman's ischæmic contracture though rare is met with in lower limb. The specimen is preserved in the Madras Medical College Museum.

The patient recovered and was able to get out well with crutches. The posterior flap method is satisfactory.

VI. *A case of a tumour under the triceps adherent to the capsule of the right elbow joint.*—Gopalakrishnan, aged 18, had an immobile circumscribed, firm tumour under the triceps with involvement of ulnar nerve on the right side; a provisional diagnosis of fibroma was made. On operation, the tumour was encapsuled, firm, adherent to the capsule of the joint and was excised with a portion of the capsule of the elbow joint which got opened into.

As the ulnar nerve was adherent, it was dissected out and an anterior transposition was done. The tumour was found on naked eye examination to be encapsuled and calcareous or cheesy in places.

Histological examination of the section showed some giant cells but not tuberculosis. The man is under observation for the last nine months. He is healthy and fit. His ulnar nerve is recovering. His elbow joint movements are perfect. The accompanying print (No. VI) shows the condition before operation.

VII. *A case of osteo-malacia.*—Osteo-malacia is seldom seen in this part of India. An obstetrician of 20 years experience in a hospital where there are 2,000 confinements a year has met with only one case and that in a Northern Indian woman.

A case is recorded from the Government Hospital for Women and Children, Madras, in the *Madras Medical Journal*, Vol. XVIII, Nos. 1 & 2, March 1938).

A Muhammadan female, aged 25, was seen in the out-patient section of the orthopaedic department for back-ache; she is a purdah woman, has three children and her labours were normal. The disability has increased after her recent confinement; she could scarcely shuffle herself along. There was the suspicion of tuberculous disease of lumbar spine or sacroiliac joint. She could only be examined with her clothing on; the spinal movements were limited to a great extent.

A radiographic examination of the pelvis and spine showed the marked changes of osteo-malacia.

In the X-ray pelvis (No. VII), there is flattening out

of the pelvic brim from the sides; there is fracture of the ascending and descending pubic ramus on either side; no coxa vara; there is generalised rarefaction of bones.

Her blood calcium (S. No. 386-7 of 28th January 1938 Medical College Bio-Chemistry Department) was 5.1 mgms. per cent and Inorg. Phosphates 2.73 mgm. per cent.

Her urine calcium was 163.8 mgs. as CaO, the total quantity of urine sent being 450 c.c. That was collected by the patient at her home. The Wassermann reaction was negative. Further observations could not be carried out as the patient refused to remain in hospital. She stopped attending the out-patient.

VIII. *Tuberculosis of Muscles.*—Keen (Vol. I, p. 659) "Tuberculosis of muscle is seldom encountered. It is almost never primary, although there are some reported cases; secondary muscular tuberculosis is seen in association with bone disease and chronic abscesses adjacent to the muscle."

Beattie and Dickson states "The psoas and lumbar abscesses are common examples of this secondary infiltration".

Boyd also mentions the rarity of tuberculosis of muscle.

Keen in Vol. II, p. 439, says "Muscles may become infected either by direct extension from

neighbouring foci of tuberculosis or by metastasis.

(1) infection by direct extension is common; it is of nodular type; examples:—tuberculous psoriasis in disease of the vertebrae; tuberculosis of the quadriceps femoris from gonitis; in disease of the sphincter, from tuberculous ulceration of anus

(2) Metastatic infection—

*Primary tuberculosis of muscle.*—Lanz and De Quervain have made a careful study of the muscle tuberculosis. Usually the local lesion is secondary to a disease in the bronchial gland. Trauma is important. The virus acts particularly in the muscular connective tissue. The muscular fibres of the involved area atrophy. The disease may be miliary or one or more solitary nodules may coalesce and form a caseating mass, which may become encapsulated.

Complete removal of the mass is important and the prognosis is good.

#### Case Report.

M., 13 years, was admitted with the following history: Two years ago patient had an injury to the left forearm. One year later developed a swelling of the middle of the left forearm. This was operated upon and it healed up. Again 2 months later another swelling appeared near the former one, and it was operated. The wound did not heal up. Sinus has been left behind discharging pus. A swelling in the belly of the right quadriceps appeared

about 3 months ago. No fever or cough. No family history of cough or fever.

Left forearm was radiographed and there was no evidence of disease or injury of the bones. There was contracture of the flexor muscles of the left forearm; the thigh swelling was aspirated, it contained pus which was sterile; the sinuses of the left forearm were enlarged, curetted; they are healing up. A section of the muscle from the forearm shows the condition to be tuberculous.

The right thigh swelling was in the substance of the rectus femoris and was dissected out entirely. The encapsulated cold abscess is 4 inches in length, thick walled and on naked eye examination the interior is studded with tubercles; on histological examination it proved to be tuberculous. The specimen is preserved in the Madras Medical College Museum.

IX. *Osteoporosis of carpal bones.*—Antony, male (Ortho. 563, 12th June, 1938), aged 20, was seen for sprain of the right wrist joint. The complaint was weakness of wrist, there was no swelling or warmth and there were no clinical evidences of inflammatory trouble.

Radiogram (No. IX) showed the lunate to be irregular, sclerosed; the joint space between os-magnum and lunate has disappeared; the os-magnum is fragmented and dense.

X. *Arthrodesis of shoulder.*—(a) Srinivasan, aged 18, was seen

for tubercle of right shoulder; Mantoux's test was positive.

An arthrodesis (Jones' operation) was performed. The radiogram shows the condition after four months. The patient could abduct up to a right angle; raising the hand above a right angle is difficult. The radiogram shows the acromion, the coronoid process and the bare head of the humerus into one solid mass.

(b) Male, 27, has right brachial plexus paralysis involving biceps; wrist movements are free; the elbow is not steady; he had a

fall three months ago from a tree. Inability to abduct the right arm, wasting of supra- and infraspinati muscles and of deltoid and triceps to some extent. Triceps normal. Pectoralis is fairly well reacting.

Electrical reactions—The right deltoid is negative to faradic stimuli; sluggish to galvanic stimuli; Right biceps weak to faradic stimuli; rest of the muscles all normal in reaction. An arthrodesis of the shoulder has been performed; the elbow requires steadying with a leather splint. The patient becomes an economically efficient man.

### REPORT OF THREE CASES OF ECTOPIC PREGNANCY

BY R. C. KRISHNAN, F.R.C.S.(I.),

*Government Hospital for Women and Children, Madras.*

*Case No. 1:*—Mrs. K., a 27 year old 5th para was admitted into the Government Hospital for Women and Children, Egmore, on 1-1-37 for acute pains in the lower abdomen. There was nothing abnormal in her previous history. Her previous labours were natural. Her last child was born six years ago. Her periods were regular. Her last period lasted from the 29th to 31st December 1936 after a period of amenorrhoea for 45 days. The discharge was black in colour.

The patient gave a history of sudden attack of pain in the lower abdomen at 12 noon on the day of admission into the hospital, while returning from the bath room. The pain was acute

and agonising. She almost collapsed.

Examination at the time of admission showed a slightly anæmic well-nourished woman with a pulse rate of 110 and a temperature of 99° F. Heart and lungs were normal.

Abdominal examination disclosed slight rigidity and tenderness over the hypogastrium and left iliac region. The flanks were not dull. Vaginal examination disclosed a soft cervix with the external os closed. Pulsation was felt in the fornices, and the size of the uterus could not be made out due to the slight rigidity of lower abdomen. No definite mass

was felt in the fornices but there was marked tenderness and bulging over the left fornix. Brownish discharge was present on the examining finger. Ruptured tubal pregnancy was suspected. The case was seen by the First Obstetrician who opened her abdomen under general anaesthesia. Free blood was found in the peritoneal cavity. Blood was found oozing from the abdominal ostium of the left tube which was enlarged (tubal abortion). The left tube was removed. Abdomen was closed in layers. On cutting open the tube, dark blood clot was noticed inside.

Three days after the operation, she complained of pain in the lower abdomen and passed a uterine cast. She made an uninterrupted recovery and was discharged cured on 22-1-37.

*Case No. 2:*—Mrs. M. R., 34 years old, was admitted into the Government Hospital for Women and Children on 6-1-37 for pain all over the lower abdomen, especially in the right iliac fossa, and flatulent distension of abdomen for a day. She had six children and the last child was born two years ago. Her periods were regular. Last period was on December 18th. She bled profusely for 14 days. There was nothing abnormal in her previous history.

Examination at the time showed a thin pale woman with a pulse rate of 112 and a temperature of 98.4° F.

Abdominal examination disclosed a rigid abdomen with hyperæsthesia over the right iliac fossa. On palpation the whole abdomen was tender, particularly so in the right iliac fossa. Appendicitis was suspected as she gave a history of attacks of pain, chronic indigestion and frequent taking of purgatives to open her bowels.

Vaginal examination disclosed a small cervix directed downwards and backwards. Body of uterus was anteverted. Left fornix was very tender. A tender lump was felt in the right fornix. There was no discharge on examining finger.

7-1-37.—She complained of vague pains in the abdomen. There was no definite localisation. There was no rigidity or tenderness anywhere. She complained of flatulent distension of abdomen. The tongue was thickly coated.

Hb. 45 per cent. Blood picture was of a secondary anaemia. Motions—round worm ova+.

8-1-37.—She gave a history of having had a colicky pain of sudden onset in the lower abdomen. She began to bleed per vaginum after that. Since then she had been suffering from vague pains in the lower abdomen.

She was seen by the First Obstetrician who on vaginal examination found the uterus enlarged and pushed to the left by a definite tender lump in the right fornix. Ectopic pregnancy was suspected and operation was

advised. The patient refused operation. Her temperature was ranging from 98.4° F. to 99.8° F. and pulse rate varying from 96 to 116.

9-1-37.—Blood count showed W.B.C. 14,400, R.B.C. 3 millions and Hb. 45 per cent Blood picture was that of secondary anaemia.

12-1-37.—She complained of severe pain similar to labour pains from the morning and bloody discharge per vaginum and also of a feeling of something obstructing her genital passage.

24-1-37.—Hb. had risen to 65 per cent B.P. 100/70. She consented for operation. Her abdomen was opened under spinal anaesthesia. There was a mass consisting of right tube, distended with a blood clot (tubal mole), right ovary and left tube and ovary behind and adherent to the body of the uterus. On separating the adhesions, dark blood escaped. Sub-total hysterectomy and double salpingo-oophorectomy was done. Abdomen was closed in layers. Pathological report of the specimens showed chorionic villi and products of conception in the blood clot found inside the tube.

She had an uneventful recovery and was discharged cured on 20-2-37.

Case No. 3.—Miss P.M., aged 16, was admitted into the Government Hospital for Women and Children, Egmore, on 11-2-37 for fever and pain in the abdomen for six days. She was unmarried.

Her periods were regular. Her last period was late by ten days and lasted for twelve days. There was nothing abnormal in her previous history. Examination at the time showed a well-nourished girl with the tongue slightly coated, a pulse rate of 100 and a temperature of 101° F. Nothing abnormal was found in heart and lungs. Abdominal examination disclosed tenderness all over the abdomen more in the left iliac fossa. There was no rigidity or dullness in the flanks.

Vaginal examination revealed a normal sized retroverted uterus displaced to the right by a tender lump in the left fornix. No pulsation was felt over the lump. There was no blood on the examining finger. She was treated conservatively and her pulse was watched.

12-2-37.—Her pulse and temperature were normal but she was still complaining of pains in the left side of the lower abdomen.

13-2-37.—Her condition was unaltered. B.P. 115/75. White cell count showed 12,900. Urine clear and there was no deposit. Breasts were secreting milk. She was suspected to be a case of ectopic pregnancy and her abdomen was opened under spinal anaesthesia. Great omentum and pelvic colon were adherent to left tube and ovary. Left tube was swollen and congested. Tubal rupture at the ampullary portion near the isthmus was seen. Left

salpingo-oophorectomy was done. Appendix which was retrocaecal, long and kinked, was removed. Abdomen was closed in layers.

Pathological report.—Fallopian tube shows evidence of acute inflammation with blood clot inside. Another bit of tissue showed evidence of products of conception. Appendix showed an abscess and blood clot.

Comment.—The first case showed a typical history of 45 days amenorrhoea, scanty uterine bleeding, black in colour, onset of sudden acute pain in the abdomen, from which she collapsed and physical signs (slightly pale, with a pulse rate of 110 and a temperature of 99° F, slight rigidity and tenderness over the hypogastrium and left iliac region, a soft cervix pulsation and marked tenderness with bulging in the left fornix) There was no difficulty in arriving at the diagnosis or any doubt about the diagnosis.

The chief symptom in the second and third cases was profuse bleeding per vagina lasting for 12 to 14 days with a history of 40 and 45 days amenorrhoea. The second case in addition had all the signs of acute appendicitis (pains all over the abdomen especially in the right iliac fossa, flatulent-distension and constipation with history of attacks of

abdominal pains and indigestion, hyperaesthesia and tenderness over the right iliac fossa). So she was treated as a case of acute appendicitis for two days. On the third day, she was diagnosed to be a case of ectopic pregnancy by the first Obstetrician from her history of 45 days amenorrhoea attacks of spasmodic pains in the abdomen with uterine bleeding for 14 days and feeling of a definite tender lump in one fornix pushing the uterus of normal size.

The third case was an unmarried girl. She was treated as a case of acute salpingitis (tongue slightly coated, abdomen tender all over especially on the left iliac fossa and a tender swelling in one fornix. A temperature of 101° F with a pulse rate of 100). She was diagnosed definitely as a case of ectopic pregnancy when the pulse rate and temperature became normal two days later with the pain and mass still persisting in the lower abdomen and breasts secreting milk. This case also had a diseased appendix which was removed, as is usually done in all laparotomies. This appendix showed an abscess in its wall.

In conclusion, my grateful thanks are due to the Superintendent of the Government Hospital for Women and Children, Madras, for permission to report these cases.

# A CASE OF RETRO-OLIVARY BULBAR SYNDROME

BY M. D. ANANTACHARI, M.B.B.S.,

General Hospital, Madras.

A man, aged 25 years, was admitted into Captain Minchin's wards in the General Hospital, Madras, for pain in the right side of face and difficulty in swallowing with the following history:

Three months before admission when he went out to the fields for his daily labour he became suddenly aware of inco-ordination in his limbs, felt very giddy and had to return home. He did not vomit at that time; neither did he notice any paralysis in his limbs. After an hour he noticed numbness of his right upper extremity and right side of face and neck.

Two months later he found that he was getting hoarse in his voice, that fluids and solids had to be swallowed with difficulty and care, as otherwise they regurgitated through the nose. He had persistent pain in the right temporal and facial regions and felt benumbed over the face and right half of the body. He also noticed that the right half of the face did not sweat as much as the left.

On admission the following was his condition:

## Nervous System:

Intelligence: Very good, more than the average for his class.

Gait: Slight stiffness in walking. No tendency to fall on any side.

Speech: Hoarse voice.

Cranial Nerves: I and II nerves not affected.

III Nerve: Nystagmus on looking towards the right, with the slow component towards the left—also a rotary nystagmus, clockwise in direction. No pupillary changes. No diplopia.

IV, VI, VII, VIII nerves normal.

V: Motor part normal. Sensation over the distribution of the right V very good to touch and tactile discrimination, but considerably diminished to pain, heat and cold.

X: The right half of the palate paralysed. Laryngoscopic examination showed paralysis of the right vocal cord. It was also noticed that there was a small nodular mass in the middle of the right vocal cord. Slight paresis of the left vocal cord. Deglutition—difficult.

IX Normal. No changes in taste, either in the anterior two-thirds or posterior third of the tongue.

XI and XII normal. No paralysis of the tongue or trapezius muscle.

Sensory changes: Complete anæsthesia in the distribution of the right 2nd and 3rd cervical nerves. There was as noted above loss of sensation to pain heat and cold over the distribution of the right V nerve.

Sensation was not affected on the left half of the body. Co-ordination and joint sense good. Vibration sense diminished on the right side and on the malleoli in the left side.

Motor changes: Except for the paralysis of the right X nerve, there were no motor changes.

Reflexes: (a) superficial: Conjunctival reflex diminished on the right side. Abdominal reflex lost in the lower quadrant on the right side. Plantar reflex, extensor on the left side and flexor on the right side.

(b) Deep Reflexes. All reflexes exaggerated on the left side. Slight clonus could be elicited on the left. On the right only the K. J. was exaggerated.

No disturbance of the bladder.

Rombergism marked.

Sympathetic: Right cervical sympathetic was affected. The patient had a constant frown on his forehead. When taken off his guard, it was noticed that his right palpebral fissure was smaller

than the left. There was no miosis. Very slight enophthalmos. Ocular tension very much diminished as compared with the left. There was no marked dilatation of the pupil on cocaineisation. Reaction to light normal. Pilocarpine injection resulted in marked sweating of the left side with a slight sweating on the right side of the face and no sweating on the right side of the neck up to the middle line.

Firm pinching of the right half of the neck produced no reaction of the pupil.

Oculo-cardiac reflex absent.

Progress: The condition was practically stationary during his stay in hospital under observation. There is no history of syphilis. No history of diphtheria W.R. of the blood negative. No enlargement of glands in the neck.

Discussion.—Paralysis of the X-nerve, dissociated anæsthesia on the right half of the face, and (partial) paralysis of the sympathetic place the lesion in the neighbourhood of the medulla or upper cervical spinal cord. Dissociated anæsthesia on the right side of the body would have completed the classical picture of the syndrome of posterior inferior cerebellar artery.

Though variations in the distribution of the arteries to the medulla are well known as instanced by J. B. Stopford in his monograph it

is rather difficult to reconcile the clinical appearances of this present case with those of instances on record, on account of the total absence of sensation in the distribution of the right second and third cervical nerves, though absence of the dissociated anaesthesia on the opposite half of the body may be anticipated if it be conceded that the spinothalamic fibres on the outer aspect of the medulla might escape in a vascular lesion of the inferior cerebellar artery.

A factor of interest is the presence of the small mass in the middle of the right vocal cord. Its role is the causation of the group of symptoms is difficult to assess.

In a review of the cases of posterior inferior cerebellar artery thrombosis. J. B. Stopford has analysed 22 authentic cases with reference to sensory changes. In no case had there been loss of sensation to all forms of stimuli on the same side as the lesion; the case placed on record here differs

in this respect. In differential diagnosis a suggestion of disseminated sclerosis is possible in which case the fleeting nature of the symptoms and a gradual onset should be characteristic. Here the group of symptoms of affection of the inferior part of sensory muscles of the V nerve and paralysis of the X nerve with affection of the sympathetic refer only to a region in medulla behind the olivary body.

It is difficult in the absence of post-mortem examination definitely to fix the nature of the lesion. A sudden onset and its limitation in progress point to vascular affection. In the absence of syphilis and arteriosclerosis such a conclusion will be unwarranted. It is for that reason that the case has been presented as one of retro-olivary bulbar syndrome and not as a case of thrombosis of any artery.

#### REFERENCES:

- (1) *Lancet*, 1934, Vol. II, p. 975.
- (2) *Lancet*, 1935, Vol. I, p. 1214.
- (3) *Journal of Anatomy*, 1925, Vol. 59, p. 120.

### MAY SOON WAIT AGAIN.

A middle aged farmer passed the old doctor on the road one day, stopped him and told him he wanted to pay him what he owed him. The doctor scratched his head for several moments trying to think what services had been rendered, and finally said, "What do you owe me for, Tom?"

"For the baby," replied Tom.

"Oh well, that will be the usual fee," and named the usual amount collected in that community.

As the farmer started to drive on, the old doctor yelled, "By the way, how is the baby?"

"She's fine, Doc,—she's going to get married tomorrow," and drove on.

D. H. P.

From J.A.M.A.

## Abstracts from Current Medical Literature

### PHARMACOLOGY.

**The Mechanism of the New Chemotherapy.** FRITZ MEYER (writing in the *B. M. J.*, April 9, 1938) believes that sulphanilamide has a direct action in the body of the bacterium destroying its structure. Sulphanilamide acts only in organisms which possess a certain amount of natural resistance. Therefore its action can only be explained as a co-operation of drug and organism. He observes that cases of severe streptococcal infection, as for instance puerperal fever, which do not respond to sulphanilamide may be cured by additional treatment with anti-streptococcal serum; the same holds true for cases not responding to serum treatment, which may recover by adding sulphanilamide. In as much as the chemotherapeutic agent can only exert its action under co-operation of the natural defence system of the infected organism, this resistance must be supported by all possible means (immune transfusions, vitamins, etc.) The toxic by-effects of sulphanilamide can be avoided by combining serum and sulphanilamide, because this combination makes the reduction of the sulphanilamide dosages below the point of danger possible.

**Nicotinic Acid in Dietary Deficiency.** H. CHICK, *et al* (*Biochem. J.*, January 1938. *Abst.*

*B. M. J.*) report the effects of administering nicotinic acid to two pigs fed on a maize-casein diet deficient in vitamin B. Both animals were losing weight rapidly, had diarrhoea and dermatitis were refusing food, and were so ill as to be expected to die within two or three days; one had a paresis of the hind limbs. Various fractions of yeast extract had no effect. Nicotinic acid was given first intramuscularly in doses of 100 mg., and then by mouth in doses of 60 mg. per day. Within 24 hours of the first injection appetite returned, and then followed a steady reversal of the former condition so that after 6 weeks' treatment the pigs appeared quite healthy.

**Calcium and Blood Coagulation.** (*J. A. M. A.*, 109, 22, dated 27th November, 1937). The essential features of the various modern theories of coagulation include a protein called prothrombin as a normal constituent of the blood. This was changed to thrombin directly or indirectly by a substance (kinase) contained in tissue fluids and platelets, when calcium is present. The resulting thrombin brings about a change of the fibrinogen, ordinarily present in blood, to fibrin, which is the basis of the clot. The point at which calcium acts is in the change of prothrombin to throm-

bin. Whether it acts merely as a catalyst or actually becomes part of the thrombin, essential for its action, has been the subject of much controversy. Ferguson has introduced a new factor into the general conception. Using carefully prepared prothrombin and cephalin (kinase) with calcium chloride, he produced thrombin the activity of which was tested on solutions of purified fibrinogen. To test for the presence of calcium in the thrombin, the latter was subjected to decalcification by oxalate or citrate or by dialysis before it was permitted to act on the fibrinogen. Thrombin can lose calcium to the extent of failure to clot the fibrinogen solution if the decalcification is carried out soon after the formation of the thrombin. If the thrombin is allowed to "age" for several hours before decalcification is attempted, the loss of the calcium no longer prevents clotting. Thus there seems to be a "calcium-containing intermediate complex" which changes to stable thrombin.

An important deduction of the foregoing observations is that the action of the decalcifying anticoagulants is rather more complex than ordinarily conceived; they may prevent clotting by actually precipitating ionized calcium before thrombin has been formed, and will interfere with coagulation by withdrawing the calcium from the complex.

#### A Stable Solution of Antimony for the Treatment of

**Kala-Azar.** L. EVERARD NAPIER, R. N. CHOUDHURI and M. N. RAI CHAUDHURI (*The Indian Medical Gazette*, August 1937.) *The new compound.*—No. 561 is a clear, sterile, colourless solution which is said to be stable. It is a pentavalent compound of antimony and it contains 20 mgm. of antimony (metal) in 1 c.cm. of solution. One c.cm. of a 5-per cent solution of neostibosan contains 21 mgm. of antimony.

Toxicologically, it is very similar to neostibosan, being slightly less toxic than this compound, milligramme for milligramme of antimony when given subcutaneously, and distinctly less toxic when given intravenously—18.5 c.c. (or 370 mgm. of Sb) per kilogramme is the lethal dose for a mouse, against 6 c.cm. of a 5 per cent neostibosan solution. Its rate of excretion in the urine is rapid, 68.5 per cent being excreted in the first twenty-four hours against 50 per cent in the case of neostibosan, and therefore, the effect is even less likely to be cumulative.

A series of ten consecutive cases of kala-azar treated by intramuscular injections of the new antimony compound, No. 561, is reported.

The immediate results were very satisfactory and there is every reason to hope that in all ten cases a cure was effected. Ten injections were given in nine cases and 8 in one case.

The injections were given on alternate days in six cases and daily in four. No untoward symptoms, either general or local, were noted in any case.

In that No. 561 is a stable compound that remains unchanged even in solution, that it can be given intramuscularly without causing any local damage to the tissues, and that, in its efficacy in the treatment of kala-azar, preliminary trials suggest that it is in the same class as neostibosan, its introduction constitutes a distinct advance in the treatment of this disease.

**Absorption and Excretion of Iron.** R. A. MCCANCE AND E. M. WIDDOWSON (*Lancet*, Sept. 18, 1937, pp. 680-684.)—

**Iron Metabolism:** Experimental Findings: No theory of iron metabolism can possibly explain all the experimental observations because many of them are mutually contradictory. There are however, certain generalisation which any satisfactory theory must be expected to cover, and which will now be discussed. Within these generalisations there may be contradictory observations on points of detail which will be neglected if they are immaterial to the main issue.

1. The faeces contain amounts of iron that vary directly with the amounts in the food, and are generally approximately equal to them:—

The whole problem of iron absorption and excretion arises from this fact, because it is impossible to tell from balance experiments or from microscopical studies how much of the ingested iron has passed through the intestine unabsorbed, and how much has been absorbed, only to be re-excreted.

2. The urine contains very little iron, and the amount is generally considered to bear little or no relation to the amount in the food:—This has been recognised for many years. According to some observers the urine of healthy men contains no iron at all. This, however, has not been the experience of most analysts. McCance and Widdowson found and increased excretion of iron in urine during and after treatment of a polycythaemic patient with phenylhydrazine. It has been shown also that after iron salts have been injected intravenously, a small percentage of this iron rapidly appears in the urine, but that excretion only continues for about 20 minutes. It is probable therefore that the kidney would readily excrete inorganic ionised iron and in variable amounts if it ever had the opportunity of doing so; that it does not do so under ordinary conditions suggests that the concentration of free iron in the plasma is always maintained at a very low level by the storage organs. In other words, the moment the concentration of free iron in the plasma rises the excess is competed for by the storage organs and the excretory organs. The former always win. It is

also generally recognised that free hæmoglobin circulating in the plasma above a certain concentration is readily excreted by the kidney.

3. The body has considerable storage capacity for iron:—

It will be observed that as so far discussed the metabolism of iron differs sharply from that of sodium.

4. It is certain that in some way iron must be transported very efficiently about the body:—During pregnancy, for instance, about 350 mg. of iron are transferred to the foetus from the mother. Again, the healthy infant is born with an excess of hæmoglobin in its blood. This excess it converts largely to inorganic iron, and it is unlikely that the conversion or the subsequent resynthesis takes place only at the sites of storage. During growth, iron must be absorbed and carried to the blood-forming organs for the manufacture of new red cells for the developing body. Between the first and the twenty-first year about 4000 mg. of iron are retained. Distributed over 20 years this amounts to an average retention of 1·8 mg. a day. Further, iron injected into animals or taken by mouth is stored in large amounts in certain internal organs, and the post-mortem findings in hæmochromatosis show that during life there must have been continuous transport of iron from the gut to various parts of the body.

In spite of the confusion about the amount and state of iron in the plasma it is natural to suppose that the plasma is the medium for the transport of iron. This view is supported by the work of Bing and others and of Heilmeyer and Plotner.

Phagocytes, leucocytes, lymph, and other media of transport which have been suggested scarcely seem sufficiently physiological or indeed efficient enough to provide for the demands of the body. This point of view and other arguments in its favour may be found set forth in a short article by Moore and Doan.

The whole question of plasma and urinary iron, their relationship to each other and their possible fluctuations during disease or treatment clearly require detailed and critical investigation. Transport by the plasma suggests that an equilibrium exists between the storage organs the plasma, and all the cells of the body. It also suggests that any variation detected in the amount of iron excreted, either by the intestine or in the urine, reflects a variation of plasma iron in the same direction. While recognising that some such generalisation as this must be true, our knowledge at present scarcely enables us to visualise the details.

5. It is apparently possible in health to maintain adults in iron balance on any intake likely to be derived from natural food-stuffs:—Earlier work, in which

negative balances were sometimes obtained, has been confirmed by Barer and Fowler but not by other recent investigators. According to Lintzel balances can be maintained, at any rate for a short time, on intakes as low as 1 mg. per day. Neither Fontes and Thivolle nor Nicolayson were able to maintain dogs in equilibrium on intakes as low as this, so that there may be special differences. There may also be age differences, for it has been shown that on their normal (small) iron intakes, babies were in negative iron balance during the first two months of life. Lintzel obtained iron balances on intakes up to 60 mg. a day, and Reimann, Fritsch and Schick found very slightly positive balances when 100 mg. of iron a day were administered to normal adults. The work of Dry, Brock and Hunter, and of Fowler and Barer strongly suggests that on intakes of 500–1000 mg. of iron a day positive balances would always be obtained. It is true that positive balances were not obtained by Muller, but a critical examination of the figures given by this author suggests that there was something seriously wrong with his technique. One patient, for example, is reported to have had 4·05 million erythrocytes, and a hæmoglobin of 80 per cent (Sahli). The blood iron was 148 mg. per 100 c.cm., and on an intake of liver plus 1·6 g. of iron daily the patient had a negative iron balance of over 2000 mg.

6. There are characteristic differences between the iron ex-

changes and the blood picture in the two sexes.—Women tend, even in health, to have less hæmoglobin in their blood than do men. Further, they are much more frequently found to be anæmic. Davidson and others in a study of the incidence of anæmia among the poorer classes in Aberdeen, found that among the men, even in low iron intakes, anæmia was conspicuous by its absence. Among the women, on the other hand, anæmia was found in nearly half the subjects. Associated with these observations, and possibly in part explaining them, is the fact that women lose 10–40 mg. of iron each month in menstruation; pregnancy and parturition result in a loss of about 400 mg.

7. Anæmias of the hypochromic type can be cured by the administration of iron, so that in these circumstances iron must be absorbed: Small doses are sufficient in normal persons and animals, and in fact the absorption and utilisation of even the small amounts of iron in food may be extraordinarily efficient under these conditions. Some anæmias can only be cured by enormous doses of iron, but it would be wrong to suppose that this is due to any failure of absorption, since it has been shown that when the intakes are high large amounts of iron are continuously being absorbed. Iron may be much better retained by anæmic than by normal persons.

8. It is believed that about 3·3 per cent of the total hæmo-

globin of the blood is destroyed every day. In a 70 kg. man this involves a katabolism of about 29 g. of hæmoglobin or 90 mg. of iron, some of which certainly passes through the inorganic state. This turnover of iron is of a very much higher order than the daily intake and output.

9. Very little or no iron is excreted during or following sudden hæmolytic anæmias: Much of the iron set free appears to be stored in the internal organs, mostly in inorganic form. The small negative iron balances obtained by Stearns and McKinlay during the period of "physiological hæmoglobin destruction" can hardly be said to contradict this, for their own figures show that there was little change in the total amount of hæmoglobin in the babies' blood.

10. There are two diseases associated with an excess of iron in the body. In *hæmochromatosis* immense deposits of inorganic iron are found in the liver, pancreas, skin and other parts of the body. Iron is not deposited in all these sites when it is forced into the body by injection. *Hæmochromatosis*, therefore, is not simply due to faulty iron elimination, although this has been suggested. It is important to note that in spite of the enormous deposits of iron in the organs there are usually subnormal amounts of hæmoglobin and of iron in the blood. In *polycythæmia rubra vera* the number of red cells and the amount of hæmoglobin are very greatly in excess

of normal, so much so that the amount of iron in the blood may be doubled. The red cells may be increased more than the hæmoglobin. In other words, there may be signs of a deficient iron supply to the blood-forming organs. This is indeed not surprising when the demands which are being made upon the iron supplies are considered. In addition to these two diseases there are others in which there may be a great excess of iron in the solid organs. Pernicious and aplastic anæmia, and Cooley's erythroblastic anæmia are good examples. It has not been proved in these instances that the total amount of iron in the body is increased. The deposition in the organs may have taken place entirely at the expense of the blood, and one must always remember that before death these cases have generally been treated with large doses of iron.

The site of absorption is the entire intestinal tract, although the duodenum and a portion of the upper intestine probably play the major role . . . . . Elimination is almost entirely by intestine, especially by the colon . . . . This theory is really a legacy of the histologists of the nineteenth century, although it has been strengthened on histological grounds from time to time, and is still generally accepted. The life and soul of this theory has undoubtedly been the fact that there is no morphological distinction between absorption and excretion. To most people the term "excreted by the intestine" un-

doubtedly implies regulated excretion, *i.e.*, that the gut performs for iron the function which the kidney performs for sodium, and with equal facility. It does not necessarily follow from this that iron is always being *freely* absorbed and excreted, but it is implied that *appreciable* absorption and excretion are always in progress. When the accepted experimental data on iron metabolism are examined in the light of this theory, certain difficulties at once arise. These difficulties are intensified by a study of recent work on the function of the intestine. Thus, while the theory explains well enough the avenues by which iron leaves the body, and the results obtained from balance experiments at moderate levels of intake, it breaks down completely when examined in the light of the following considerations:—

(a) Extensive intravital hæmolysis, however brought about, which is known to set free large amounts of iron in the body, does not appreciably increase the excretion.

(b) When iron is injected into rats in such amounts that the normal iron content of the body is doubled, trebled or more, practically the whole of the injected iron may be recovered from the organs. Gottlieb's solitary experiment showing that guinea-pigs do excrete injected iron by the bowel, is still awaiting confirmation. If corroborated, it suggests species differences.

(c) If the body ever tended to excrete unwanted iron, it is diffi-

cult to explain why one should find such large quantities of free iron stored in the livers of patients who have died of pernicious anæmia. The iron has not been required for the formation of hæmoglobin (in such amounts) for many years. One would have expected, therefore, that it would have been slowly excreted if any organ of the body had the capacity or opportunity for doing so.

(d) If appreciable absorption takes place from the intestine every day and is followed by regulated excretion, it is not easy to see why simple anæmias only appear to arise when there is some drain on the body iron. Thus, men are very rarely anæmic unless there is some chronic source of blood loss. Women are frequently anæmic, and there is evidence that the lower hæmoglobin level of so-called "normal" women may be pathological rather than physiological. Why should this be so? Granted that their intake of iron is lower than that of men, and that they lose about 20 mg. of iron each month during menstruation, they have to absorb less than 1 mg. of iron a day to make good this loss. Surely the poorest of diets is sufficient to supply this. Again, why is anæmia so prevalent in women who have borne children if appreciable amounts of iron are absorbed each day? If the intestine regulates iron excretion it should be able to conserve the body iron. The foetal demands for sodium, which are supplied from the maternal blood, do not

make the mother sodium deficient, even if her sodium intake is low, for her kidney conserves her body sodium exactly to the extent required.

None of these observations suggests an active regulatory excretion. Further, the best chemical work indicates that the large intestine does not excrete iron in appreciable quantities and takes no part in regulating the amount of iron in the body. This throws the onus of regulation of iron excretion on to the small intestine, but even this is rendered most improbable by Nicolayson's experiments on dogs with isolated colons. In these animals no extra excretion of iron by the small intestine followed the daily injection of 67 mg. of iron.

*A new theory of iron metabolism.*—While admitting at once that some of the iron in the faeces must come from excreted juices and abraded cells, and also that the amount and variability of the iron so excreted may vary widely from species to species, it is suggested on the basis of work already referred to that in man the quantity of iron lost in this way is small and constant (see also Christiansen). Taken together with the accepted facts about the excretion of iron in the urine, it follows that the total excretion of iron is small and relatively fixed in amount.

Now obviously negligible and non-regulatory excretion, even with great storage capacity, must be coupled with limited and

to some extent controlled absorption. The factors governing absorption must therefore be considered, and the simplest possible theory has been accepted in the first instance as the working hypothesis. The possible effects of calcium, phosphorus, hormones or vitamins on iron absorption or excretion will not be considered in any detail. The same applies to the effect of the thyroid hormone or vitamin C on hæmatopoiesis, and sexual differences in the storage of iron. It is accordingly suggested that the absorption of iron is conditioned mainly by the relative concentrations of free ionised iron in the intestine and in its epithelial cells.

The cells may actively prevent the outward diffusion of iron into the lumen, but in any case passage in this direction is probably very small for two reasons. Firstly, the concentration of free iron in the plasma, and hence probably in the intestinal cells, is always very low and maintained so by the efficiency of the storage organs. Secondly, it may be assumed that there is always some iron in the intestinal canal because all the secretions which are poured into it probably contain iron, and in the case of the bile this is certainly true. Hence the diffusion gradient from cells to lumen can never be a steep one. *Vice versa*, practically no iron will be absorbed if the intake is very low because the concentration of free iron—at any rate in the small intestine—will never rise much above that of the free iron in the cells. Since, moreover,

iron is divalent or trivalent it is probable that it passes through the cells only with difficulty in either direction (compare  $\text{SO}_4$  and magnesium and calcium). Thus, small differences of concentration may develop and even be maintained for a time without appreciable passage of ions.

It follows from these considerations that the balances of intake and output that have been observed at physiological levels of intake are brought about by the absence of any significant absorption or excretion. With intakes large enough to be quite outside the physiological range positive balances would be expected and this has in fact been shown to be the case.

It is suggested, therefore, that iron is excreted in very small amounts both by the bowel and kidney. The smallness of the excretion is due to the fact that the activity of the storage organs constantly maintains the plasma iron at a low level. It is doubtful whether the intestine has any power of regulating iron excretion. Iron is not freely absorbed. The amount absorbed depends upon the relative concentration of free ions in the lumen of the gut and in the cells and plasma. At physiological levels of intake only a very small fraction of the ingested iron is absorbed.

The new theory explains satisfactorily the observations which, as has already been shown, are difficult to reconcile with the current theories. Thus one would

not expect to get much increased excretion of iron after intravital hæmolysis or after the injection of inorganic iron.

Since, under normal conditions, the human body is now considered to excrete practically no iron, the menstrual loss at once assumes a significance which was difficult to assign to it on the older theories. Women tend to be genuinely short of iron, and the shortage is accentuated by their low iron intakes. They are living, therefore, at a lower plane of iron metabolism than men. Additional iron by mouth raises the absorption from their intestines and their hæmoglobins reach a higher level. The theory similarly explains the hypochromic anæmias of multiparæ in whom the demands of pregnancy and parturition have more than replaced the menstrual loss. One must always bear in mind, however, the possibility that the tendency to anæmia in women may be accentuated by other factors. They may utilise the small amounts of iron which they do absorb rather differently from men.

Further, the new theory accounts reasonably well for the positive balances observed on normal intakes after hæmorrhage and the positive balances which must occur to produce the accumulations of iron which take place in polycythæmia and hæmochromatosis. After a hæmorrhage or in polycythæmia the activity of the marrow so reduces the concentration of iron

in the body cells and plasma that diffusion from the gut is sufficiently facilitated to allow appreciable absorption to take place. In hæmochromatosis the iron deposited in the cells is insoluble and inert, and takes no part in the general equilibrium. Hence there is a true deficiency of free iron, as evidenced first, by the anæmia, and secondly by the cure of the anæmia by the administration of iron.

The absorption of iron during childhood may be explained along similar lines. The growing body and the active marrow maintain the concentration of free iron in the plasma and epithelial cells so low that absorption is appreciable with normal intakes. It remains to explain why absorption should become so much slower after the growth period. It is suggested that this is brought about by the rise of free iron in the epithelial cells consequent upon the reduced demands for cell and hæmoglobin formation. An increase of iron in epithelial organs at or about maturity has in fact been shown to take place by Zondek and Karp, so there is experimental support for this view.

An important aspect of iron metabolism is the necessity for giving quite unphysiological doses of iron to cure certain anæmias common in clinical practice. Recent work suggests that after treatment has been in progress for a short time there must be abnormally large amounts of iron in the body. It is tentatively suggested that

these patients and those with *polycythmia rubra vera* represent the opposite extremes of normality in marrow reactions to iron. In polycythaemia the marrow is overactive and hæmoglobin is too readily formed in the presence of normal, or even subnormal, amounts of free iron in the cells and plasma. How this could lead to the continuous absorption of iron has already been discussed. In the refractory secondary anæmias, the marrow is sluggish and can only be goaded into activity by the presence of high concentrations of free iron, and, owing to the activity of the storage organs, these can only be maintained by the continuous ingestion of huge doses. It is to be noted that this theory does not suggest any reason for the activity or sluggishness of the marrow.

**Conclusion:**—As already stated it is quite impossible to evolve a theory to cover the absorption and excretion of iron which does not conflict with some of the published findings. The present theory is clearly open to criticism on many points and is likely to be so criticised. It is put forward, however, not with any suggestion of finality, but because it seems to offer a better explanation of the experimental and clinical findings, taken as a whole, than any other, and also because it indicates a number of points which clearly require investigation.

**Summary.**—It is suggested from a study of the literature

that the capacity of the bowel to excrete iron has been exaggerated, particularly its capacity to regulate the amount of iron which it excretes. There are indeed indications that in man and certain animals the bowel excretes practically no iron. If this is the case, the amount of iron in the body must be regulated by controlled absorption. The possibility of this and some of the factors likely to be concerned are discussed.

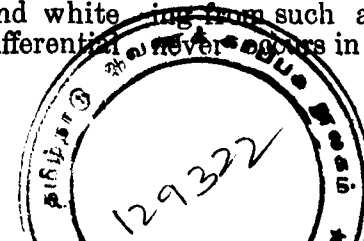
### **PATHOLOGY.**

**The Clinical Pathology of Hæmorrhagic States,** S. C. DYKE, (*B. M.J.*, October, 9, 1937, pp. 692-694). The development of the hæmorrhagic state depends upon the escape of the red cells through the unbroken capillary wall; it may result from various causes. For the determination of the prognosis and the initiation of appropriate treatment accurate diagnosis is desirable. In none of the hæmorrhagic states can this be made without the assistance of laboratory methods; in few of them, however, can it be established by laboratory methods alone. Usually it calls for the intelligent consideration of both laboratory and clinical data.

The first step in the laboratory investigation of any case of the hæmorrhagic state will consist in the examination of the blood picture. This, as usually understood, comprises an estimation of the hæmoglobin percentage, an enumeration of the red and white cells of the blood, a differential

count of the white cells, and a report on the morphological characteristics of the formed elements of the blood—the red and white cells and the platelets. For the satisfactory investigation of the blood picture it is highly desirable that the specimens for each of the examinations mentioned should be taken in the appropriate manner straight from the patient. Preparations made from specimens of blood collected for transmission into oxalate or any other anti-coagulant are usually unsatisfactory and often are quite useless.

**Bleeding time.**—In the act of taking the specimen of the blood valuable information may be gained as to the bleeding time. No satisfactory quantitative method exists for this determination. Using a large-sized, bayonet-pointed surgical needle and making the puncture after slight massage in the lobe of the ear, the bleeding normally stops well within a minute; usually it is necessary to use a little force to express drops of blood after the first two or three minutes. If after the first two or three drops the blood continues to exude the bleeding time may be taken to be prolonged. In certain cases associated with gross platelet deficiency, such as thrombopenic purpura (*purpura hæmorrhagica*), aplastic anæmia, and lymphatic leukæmia, the bleeding from a simple puncture may persist for many minutes—if unchecked—even for hours. Prolonged bleeding from such a small puncture never occurs in hæmophilia, and



may at once be held to exclude that diagnosis.

**Blood Picture.**—In those cases in which lymphatic leukæmia is the cause of the development of the hæmorrhagic state the preliminary examination of the blood picture will serve to establish the diagnosis. The discovery of the typical blood picture in a patient suffering from hæmorrhagic purpura often comes as a surprise; it is too often forgotten that lymphatic leukæmia may exist in the complete absence of enlargement of the lymph nodes or spleen. A low white cell count does not in itself serve to rule out this diagnosis: the morbid state which is the basis of lymphatic leukæmia may exist without the escape of the abnormal white cell into the blood stream. Such cases will present the clinical picture of anæmia with hæmorrhagic manifestations but with a marked diminution of the white cells. Such white cells as are present in the blood stream will be mainly of the lymphocytic order. Frequently there may be pyrexia and gangrene of the mucous membrane of mouth or gums; in such cases the differential diagnosis from agranulocytic angina may be almost impossible, short of examination of samples of bone marrow obtained by sternal puncture; and it is very doubtful whether this procedure should play any part in the clinical diagnosis of the hæmorrhagic states.

**Blood platelets.**—In the absence of any abnormalities,

either morphological or numerical, of the white cells attention must be directed to the appearance of the platelets in the stained film. If such films show few or no platelets, and especially if such examples as appear are larger than normal, the possibility of thrombopenic purpura (purpura hæmorrhagica) presents itself. If films show abundant platelets this possibility may be set aside.

Assuming that the films show apparent diminution or absence of platelets, their enumeration is called for. For this purpose many techniques have been devised. A good one is to prick the finger through a drop of 2.5 per cent sodium citrate solution in normal saline. The mixed drop of blood and diluent is rolled into a wax-lined Widal tube half-filled with the same solution. By means of a wax-lined pipette a drop of the diluted blood is transferred to a slide, covered with a slip, and ringed with vaseline. Using an oil-immersion objective, the platelets are counted against the red cells. From the number of red cells per c.mm. the number of platelets may readily be calculated. In my experience a platelet count of over 50,000 per c.mm. serves to exclude purpura hæmorrhagica as a cause of bleeding.

A blood picture showing in the face of purpura and other manifestations of an established hæmorrhagic state no morphological abnormalities of the white cells and the presence of platelets

in relatively normal numbers will suggest the possibility of an anaphylactoid condition of the Schoenlein or Henoch type. A history of preceding urticaria or the presence of arthritic manifestations will be deciding factors. The platelets may be deficient, but on enumeration will never be found to be below 60,000 per c.mm. in purpura of anaphylactoid type.

**Scurvy.**—A blood picture normal except for anæmia, with a clinical history on the basis of which both purpura hæmorrhagica and idiopathic purpura can be eliminated, especially if occurring in a young child, should arouse suspicion of scurvy. Fully developed scurvy is now a rarity; but it still does occur, and not always among the more needy strata of the population. I have seen one case in the baby of a well-to-do family of which both the mother and father were University undergraduates. The child had been entrusted to the care of an old family retainer who had many years ago acquired and still steadfastly maintained faith in one of the earlier brands of proprietary infant foods. The condition is not unusual in adults as a result of prolonged adherence to a diet of milky slops for the treatment of gastric discomfort, often diagnosed as peptic ulcer and usually nervous dyspepsia.

The work of Harris and Ray (1935) and of Abbasi, Harris, Ray and Murrack (1935) appears to offer a means of diagnosis subscor-

butic states. According to these authors the body should naturally maintain a reservoir of vitamin C. If this reservoir is properly filled a large proportion of a massive test dose of the vitamin will be excreted in the urine; failure to excrete the major part of a suitable test dose within 24 hours indicates a state of vitamin C deficiency, otherwise latent scurvy. The test presents no particular difficulty. The ascorbic acid may be given either orally or parenterally in the form of "redoxon" (Hoffmann-La Roche). The titration of the excreted acid in the urine by means of the dichlorophenol-indophenol reagent is readily carried out. Using reagents kindly supplied by Messrs. Hoffman La Roche, Dr. Freida Young has in my department at the Royal Hospital investigated a number of patients suffering both from hæmorrhagic and from other conditions. Reduced excretion was found in many cases, hæmorrhagic and otherwise; in fact, two patients—no matter what their condition—satisfied Harris and Ray's standards for the normal. We were forced to the conclusion either that a large part of the Hospital class population of this country is suffering from latent scurvy or that the standards for normal excretion are still to be established.

**Coagulation time.**—The estimation of the coagulation time of the blood is, next to the general examination of the blood picture, the most important procedure in the clinical pathology of the hæm-

orrhagic state. In spite of its importance the technique remains very imperfectly standardized; a number of methods are available. In order to obtain comparable results it is essential that the observer should adopt one method and follow it closely. The capillary tube system of Dale and Laidlaw (1911-12) is handy, and has the advantage that the observations are made in a water bath at a temperature of 37° C. By this procedure, however, the clotting time is very short: Dale and Laidlaw regarded one minute forty-five seconds as being the mean of the normal, with only slight variation on either side. This method has the disadvantage that even in morbid states in which the clotting time is increased the actual extension shown by it is not great; thus in a case of hæmophilia in which the test-tube clotting time was half an hour, by the capillary tube it was only four minutes. The older method of Lee and White (1913), though not so convenient, gives more readily comparable results. Blood is taken from a vein by means of a syringe previously rinsed in saline and is transferred in amounts of about 1 c.cm. into test tubes of 8 mm. bore, also previously rinsed with saline. Timing them with a stop-watch, the test tubes are alternately rotated about their short axes at half-minute intervals. "That point is taken as the end point at which the blood no longer flows from its position but maintains its surface contour". It is important that the tubes be not stoppered; this

decreases the coagulation time. The originators placed the normal limits as from five to eight minutes. I should be inclined to extend the upper limit of normal to ten minutes.

In addition the coagulation time varies inversely with temperature; Dale and Laidlaw showed that this acceleration of clotting is much more rapid at temperatures of over 25° C than below. For practical purposes, in the temperate zone the test of Lee and White may be carried out at room temperature. Accurate estimation of the coagulation time is of great importance in the investigation of suspended hæmophilia. The history, both personal and family, provides valuable information, but it is the prolongation of the clotting time that clinches the diagnosis.

*Post-operative Haemorrhage.*—Estimation of the coagulation time is of particular importance when surgery is in prospect. In cases of hæmophilia, when in the course of a natural remission or after blood transfusion the coagulation time by the method of Lee and White has been brought down to twelve minutes, the risk of serious and uncontrollable hæmorrhage at operation is negligible.

In cases of jaundice, other than those of the "acholuric" type associated with hæmolysis, the coagulation time may be prolonged, and its estimation will give valuable information as to the risk of post-operative hæmorrhage.

hæmorrhage. A delay in the coagulation time of anything over fifteen minutes by the method of Lee and White indicates the likelihood of inefficient natural hæmostasis. The serum calcium in these cases of obstructive or overflow jaundice is not as a rule diminished, and may even be somewhat increased, but that this tendency to uncontrollable hæmorrhage is associated with a shortage in the blood of calcium ions available for the clotting process may be demonstrated by the "calcium *in vitro* test" of Lee and Wincent (1914). This consists in adding three drops of 1 per cent.  $\text{CaCl}_2$  solution to 1 c.cm. of freshly drawn blood. In blood in which delay of coagulation is due to the presence of bile salts this procedure brings about a marked diminution of the clotting time. In cases in which the delay is due to other causes it is without effect. In this type of case both blood transfusion and the parenteral injection of calcium salts, for which purpose many excellent preparations are now available, will quickly bring about the disappearance of hæmorrhagic manifestations and reduce the clotting time to normal. Once this has been done there need be no fear of unusual post-operative bleeding.

It is important in all cases of jaundice, to bear in mind that the tendency to bleeding and the delay of the coagulation time may not depend solely on deficiency of available calcium ions. In certain cases of gross hepatic disturbance, such as are met with

in phosphorus or chloroform poisoning or in acute yellow atrophy or cirrhosis of the liver, interference with fibrin formation may occur. In such cases the coagulation time may be normal, but the clot when formed will be of poor quality; severe post-operative bleeding may then take place despite a normal clotting time, and little can be done to remedy matters.

*Nephritis.*—In nephritis the hæmorrhagic state may develop and may prove extremely troublesome. It is not an early manifestation, but may present itself in the middle or later stages of subacute glomerulonephritis. In such cases there may be epistaxis, bleeding from the gums, and a tendency to easy bruising, but purpura does not occur. Examination of the blood picture will show a simple anæmia only; pointers to the diagnosis will be found in a raised blood pressure and albuminuria. The blood urea may or may not show significant increase at this stage, but the van Slyke urea-clearance test will already show gross impairment of renal function. The hæmorrhagic manifestations are of very grave significance, but the ultimate fatal issue may be postponed for months and even for years after their appearance. In the later stages of chronic nephritis of the arteriole sclerotic type manifestations of the same symptoms in a much more severe form and with actual purpura may arise; hæmorrhage from the nose or bowel, stomach or uterus, may be profuse and

intractable. Those fulminating manifestations are terminal; the blood urea at this stage will be found to be at a level of 300 mg. per 100 cm. or more, and death is not long postponed.

It is tempting to associate these hæmorrhages with the lowering of the serum calcium, which is invariable in the developed uræmic state. In the earliertype of case, however, the serum calcium is not found to be diminished and neither in those cases nor in the later terminal state in which the serum calcium is grossly below normal do parenteral injections of calcium have the same effect as in hæmorrhage associated with jaundice.

The hæmorrhagic state may present itself in the course of many acute infections and septic conditions. In these cases its establishment appears to be due to damage sustained by the capillary walls as a result of the infection. The differentiation of cases having an infective basis from those mentioned above seldom presents any great difficulty; their clinical pathology is that of the causative infection.

### MEDICINE

**A Six-year study of the Clinical Efficacy of various Digitalis Preparations.** (*J. A. M. A.*, Vol. 109, No. 22, dated November 27th, 1937.)

**Indications.**—More than a hundred years ago digitalis lost

favour as a therapeutic agent because of its inability to slow tachycardias due to fever, and yet to-day many physicians prescribe digitalis with the hope of slowing rapid heart action due to fever, thyrotoxicosis, hypersensitivity of the sympathetic nervous system and peripheral circulatory failure. This practice is especially common in connection with surgical procedures, digitalis being given post-operatively in some places almost as a matter of routine.

Needless to say, digitalis proves of no advantage in the treatment of such conditions except in certain cases of thyrotoxicosis accompanied by cardiac disease of different etiology (such as rheumatic valvular defect associated with congestive heart failure) or in cases of pneumonia complicated with auricular fibrillation or auricular flutter. As shown in the study of pneumonia at Bellevue Hospital, digitalis when indicated in the treatment of this disease should be given only in divided doses, since massive doses may prove distinctly dangerous.

During the last two decades, several investigators have called attention to the differential diagnosis between circulatory failure due to disease of the heart and circulatory failure resulting from collapse of the peripheral vascular system. As described by Harrison, "The clinical picture of the peripheral circulatory failure (shock, collapse) is characterized by weakness as the chief subjective phenomenon, and by

ashen pallor, cold clammy skin, tachycardia, weakness of the pulse, diminution in systolic pressure". In emergencies of this character, digitalis proves of but little—if any—benefit, and, through recognition of this fact, the formerly rather prevalent procedure of administering this drug post-operatively (in ridiculously small doses) to patients with circulatory failure of peripheral origin has been abandoned. Digitalis is seldom indicated in emergencies unless there is definite evidence of right or left ventricular failure, and then in order to secure clinical benefit within a few hours large doses are necessary.

Although some clinicians still question the statement that proper digitalization improves tonicity and contractility of the myocardium, it is our opinion that the therapeutic benefit of digitalis is effected in one or all of three ways, as follows:

(1) By slowing the heart rate, that is, by lessening the number of ventricular systoles per minute, the diastolic period is lengthened, whereby ventricular filling is rendered more complete, and the heart muscle fibres are afforded more rest; and, as a consequence, there may result a greater expulsion of blood into the circulation with each systole...

(2) By increasing the cardiac tone, thereby relieving or preventing dilatation of the heart chambers beyond the physiologic limit, the optimum cardiac out-

put is made possible. When the length of the heart muscle fibres is increased beyond a certain limit, the cardiac output is decreased and "heart failure" is believed to result. Restoration of the fibres to a shorter length is a factor in bringing about an increase in cardiac output, with the possible return of circulatory efficiency.

(3) Through increase of the extent of ventricular contraction, there tends to be an increase in cardiac output when heart failure is present.

If the effects mentioned are to be expected from digitalization, the question arises as to when in the course of progressive cardiovascular disease the patient should be digitalized. Christian expressed the opinion that, as soon as a diagnosis has been made of cardiovascular disease (particularly hypertension or valvular disease) which may place an additional burden on the myocardium, the patient should be digitalized and digitalization should be maintained throughout the remainder of life. On the other hand, Harrison and Leonard (in a study of dogs) and Burwell, Neighbors and Regen (in a study of human beings) found that a reduction in output of the normal heart occurs with full digitalization. Certain studies suggest that if the heart is normal or has perhaps a slight degree of dilatation and hypertrophy, digitalis lessens the efficiency of the heart muscle and also decreases the flow in the coronary arteries. The same

studies indicate that there may be a stage in the progressive dilatation and hypertrophy of a labouring myocardium at which digitalis seems to improve the efficiency of the heart muscle and also the flow from the coronary sinus into the heart. Hypertrophy and dilatation unchecked tend toward a point where a certain optimal length of the fibres of the heart muscle is exceeded and a decrease in cardiac output results (described by Starling as the law of the heart), with gradual or sudden development of signs of heart failure. On the basis of this hypothesis, it is the physician's responsibility to estimate—through the patient's history, the physical appearances, electrocardiographic and X ray studies and his knowledge of the usual progression of the various cardiovascular diseases—just when the stage has been reached at which digitalization will preserve optimum cardiac output through increase of tonicity and extent of ventricular contraction.

It is our belief, therefore, that in the treatment of patients with progressive chronic cardiovascular disease digitalization should not be started as a matter of routine at the time of diagnosis but when, in the opinion of the physician, the pathologic processes have progressed to a point where digitalization may increase ventricular output and improve coronary flow.

*Method of Administration.*—The vast majority of patients can

take digitalis by mouth. The emetic action of digitalis is not due to a direct irritant action on the gastric mucosa but is a reflex effect from the direct action of the drug on the heart (the impulses passing from the heart to the vomiting centre in the medulla). Intravenous digitalis therapy is seldom indicated. Subcutaneous administration is necessary only in the presence of vomiting or unconsciousness or when the patient is unable to swallow. Rectal administration is seldom necessary.

It is generally admitted by physicians with experience in both methods of administration that tablets, capsules or pills of powdered digitalis leaves are much more practical than the tincture. In the first place, such preparations seem to maintain their potency better than the tincture, and, in the second place, the dosage is much more accurate, since even with the standard minim dropper the patient is apt to miscount the number of drops. The impossibility of accurate dosage in the absence of a standard minim dropper is well known to all who have tested the average medicine dropper supplied by the drug store. Furthermore it is more convenient to carry tablets, capsules or pills than a bottle of the tincture.

According to our experience the large dose method of administering digitalis is seldom necessary. In emergency cases when there is vomiting, full digitalization can be accomplished with

tablets of standardized digitalis (or their equivalent in glucose preparations) when given by mouth, in from  $4\frac{1}{2}$  to 6 grain (0.3 to 0.4 gm.) doses every six hours, within twenty-four to thirty-six hours. In the average case of congestive heart failure, complete digitalization can be accomplished in from forty-eight to seventy-two hours by administration of 3 grains (0.2 gm.) of digitalis three times a day. For an ambulatory patient with heart failure of mild or moderate degree, full digitalization can be accomplished for six or seven days by a  $1\frac{1}{2}$  grain (0.1 gm.) tablet given three times a day. After digitalization it has been our experience that the average maintenance dose is about  $1\frac{1}{2}$  grains daily. Of course some patients may require slightly larger doses, while in other instances the maximum effect is maintained by means of considerably smaller doses, even as little as one-half grain (0.03 gm.) daily.

In summary then,  $1\frac{1}{2}$  grains of a properly standardized tablet, capsule or pill of digitalis leaves is equivalent to 15 minims (1 c.c.), or approximately 45 drops, of a well standardized tincture. In general physicians are finding the tablet, capsule or pill a much more convenient form for administering digitalis than the old fashioned tincture. It is necessary to use between 18 and 30 grains (1 and 2 gm.) of digitalis to digitalize fully the average adult patient. Except in emergencies our usual routine is to give the patient

$1\frac{1}{2}$  grains of powdered digitalis four times a day (6 grains daily) for three days. Thus with a total of 18 grains we approach full digitalization with little danger of toxic symptoms. From then on the daily dose is determined by the condition of the patient's circulation and the development of toxic symptoms. The average daily maintenance dose of digitalis is between one-half grain and 3 grains a day.

**Diagnosis and Treatment of Hæmatemesis.** J. L. LIVINGSTONE (*Practitioner*, April 1935, cxi, No. 4).—It is impossible to gauge at the onset if the bleeding will be slight or severe. The prognosis in hæmatemesis is always graver than in melæna alone, as the vomiting is usually brought about by a considerable volume of blood collecting in the stomach. The cause of the hæmatemesis is sometimes obvious from the history and clinical examination; in many instances, however, it is quite impossible to make a definite diagnosis during the active bleeding and even at a later date the X-ray and gastroscope may not demonstrate ulcers or gastric erosions which have healed. The practitioner is advised to treat all cases of hæmatemesis as due to peptic ulceration until proved to the contrary.

**Mortality.**—Cullinan and Price (1932) state that a single hæmorrhage was rarely fatal (4 per cent), but that the mortality rises with one recurrence (40 per cent), and with more than one re-

currence (60 per cent). Most will admit the seriousness of recurrent hæmatemesis but Cubitt (1937) and Black (1937) quote two cases of multiple recurrences saved by massive blood transfusion.

Amongst the fatal cases a small number die within a few hours from exsanguination, but the majority linger on for 2 or 3 days, finally dying in a condition of shock. Deprivation of fluids and food, exposure to cold and anæsthesia increase the shock. A raised blood urea, proportionate to the degree of hæmorrhage has been observed. A figure of 75 mg. per 100 c.c. is said to be indicative of severe hæmorrhage.

*Treatment.*—The treatment may be summarised as follows:—

(1) Wrap the patient up warmly on a couch and give morphine,  $\frac{1}{4}$  gr., and atropine,  $\frac{1}{75}$  gr., at once. Make arrangements for transfer to hospital as stretcher case. An hourly chart is to be kept. Ice may be sucked.

(2) In two to four hours, when the patient has recovered from the primary shock, he should be undressed and put to bed with the minimum of disturbance; if

vomiting or retching persist a further injection of morphine,  $\frac{1}{4}$  gr., and atropine,  $\frac{1}{100}$  gr., should be given; the latter may be repeated every six hours and the former as required. The blood pressure should be taken and it is wise to repeat this twice daily at least.

(3) After six hours, administration of fluids per rectum should be started, with a Murphy vulcanite rectal nozzle, which should be left *in situ*; one pint of tap water or normal saline should be run in slowly for one hour, followed by an hour's rest; if tap water does not cause discomfort, it is well to alternate this with normal saline and aim at a total of six to ten pints in 24 hours.

(4) After 8 hours, the Witt's diet (*see below*) should be commenced, two hourly, the feeds being given at blood heat. The patient should be encouraged but not forced to take the feeds. If thirst is marked, sips of water or half-strength normal saline may be taken up to 5 oz. per hour. An extra feed of milk (5 oz.) may be given at alternate hours if the patient complains of hunger. *Magsorbent*, 30 grs., is given in a little water after alternate feeds.

## PROFESSOR L. J. WITT'S DIET.

Arranged for two-hourly feeding.

| Feeds per day | Food.                                                                                            | Day                                     |                                         |                                                 |
|---------------|--------------------------------------------------------------------------------------------------|-----------------------------------------|-----------------------------------------|-------------------------------------------------|
|               |                                                                                                  | 1                                       | 2                                       | 3 and subsequent                                |
| 1             | Whole milk (fresh or dried)<br>Patent barely or strained porridge                                | 5 oz.<br>Portion                        | 5 oz.<br>Portion                        | 5 oz.<br>Portion                                |
| 2             | 1 Egg beaten up in milk<br>Buttered rusks or cream crackers                                      | 5 oz.<br>...                            | 5 oz.<br>1 oz.                          | 5 oz.<br>2 oz.                                  |
| 3             | Whole milk<br>Marmite to taste<br>Barley sugar<br>Thin crustless white bread and butter slices   | 5 oz.<br>...<br>1 oz.<br>...            | 5 oz.<br>...<br>1 oz.<br>1              | 5 oz.<br>...<br>1 oz.<br>2                      |
| 4             | Strained orange or tomato juice<br>Vegetable puree<br>Pudding<br>Cream<br>Boiled or steamed fish | 1 oz.<br>Portion<br>1 oz.<br>...<br>... | 1 oz.<br>Portion<br>1 oz.<br>...<br>... | 1 oz.<br>Portion<br>1 oz.<br>Portion<br>Portion |
| 5             | 1 Egg beaten up in milk<br>Barley sugar<br>Buttered rusks or cream crackers                      | 5 oz.<br>1 oz.<br>...                   | 5 oz.<br>1 oz.<br>1                     | 5 oz.<br>1 oz.<br>2                             |
| 6             | Whole milk<br>Fruit puree<br>Pudding<br>Cream<br>Thin crustless white bread and butter slices    | 5 oz.<br>Portion<br>"<br>...<br>...     | 5 oz.<br>Portion<br>"<br>1 oz.<br>1     | 5 oz.<br>Portion<br>"<br>1 oz.<br>2             |
| 7             | 1 Egg beaten up in milk<br>Black treacle or barley sugar<br>Buttered rusks or cream crackers     | 5 oz.<br>1 oz.<br>...                   | 5 oz.<br>1 oz.<br>1                     | 5 oz.<br>1 oz.<br>2                             |

| Feeds per day               | Food.                                       | Day              |                  |                  |
|-----------------------------|---------------------------------------------|------------------|------------------|------------------|
|                             |                                             | 1                | 2                | 3 and subsequent |
| 8                           | Whole milk<br>Fruit puree<br>Pudding        | 5 oz.<br>Portion | 5 oz.<br>Portion | 5 oz.<br>Portion |
|                             |                                             | "                | "                | "                |
| Feeds at night (when awake) | 1. Whole milk<br>2. 1 Egg beaten up in milk | 5 oz.<br>5 oz.   | 5 oz.<br>5 oz.   | 5 oz.<br>5 oz.   |
| Between feeds               | Strained orange or tomato juice             | 1 oz.            | 1 oz.            | 1 oz.            |
|                             | Approximate Caloric value                   | 2,545            | 3,118            | 3,624            |

(5) After 24 hours, the hæmoglobin should be estimated and repeated every twelve to twenty-four hours, depending on the progress of the case. The blood urea should also be estimated, and if above 75 mg. per 100 c.c. should be repeated every day till the bleeding has ceased.

(6) After 48 hours, ferri et amm. citras, 30 grs. flavoured with orange syrup is given three times daily.

(7) After the 3rd day the patient is put on the routine Maclean, Sippy or Lenhartz regime for gastric ulcer.

(8) Blood transfusion of one to two pints is given on the following danger signals:—(a) pulse rate above 140, (b) systolic blood pressure below 90 mm., (c) hæmoglobin below 40 per cent, (d) blood urea above 100 mg. per 100 c.c.

(9) If hæmorrhage recurs, further atropine with or without morphine should be given, mouth feeding should be stopped for six to eight hours and then restarted as for the first day. A blood transfusion may be required.

(10) If, in spite of these measures, bleeding continues or alarming recurrences take place, a massive blood transfusion should be given.

(11) If, in spite of this, bleeding continues after two days, from the onset of the hæmorrhage, surgical intervention should be considered, but only if the hæmoglobin can be raised to 70 per cent by transfusion.

(12) In all cases known to have a chronic gastric ulcer, surgical intervention should be considered, if the hæmorrhage does not cease in 24 hours.

**Infantile Convulsions.** RICHARD ELLIS (*Practitioner*, April 1938, p. 407). Convulsions should essentially be regarded as symptomatic—the reaction of a relatively immature and unstable central nervous system to a large number of stimuli, and though certain principles of therapy will apply to the immediate attack, treatment must ultimately be based on an understanding of the cause.

**General Treatment.**—A hot bath at onset can be safely recommended. An ice cap or cold compress to the head can be used. Of sedatives, chloral and bromide are frequently effective if given in adequate dosage. If it cannot be given by mouth a rubber catheter may be passed down into the stomach and the drug given thus or double the dose can be given per rectum. As much as 7 grs. of chloral hydrate may be necessary in a new born infant. Morphine derivatives are best avoided owing to danger of respiratory failure. Mag sulph. intramuscularly has been found effective. A 25% solution of crystallised Mg. SO<sub>4</sub>: 7H<sub>2</sub>O being used, the dosage being 1 c.c. per kgm. body weight. As respiratory failure may sometime occur it is advisable to have handy the antidote (2½% CaCl<sub>2</sub> in normal saline, 1 c.c. per kgm.) A purge, calomel, or castor oil or enema should be given at once if these has been previous constipation. Anæsthetics like chloroform or ether are not advisable in single convulsions but if these occur in rapid succession the child

should be anæsthetised between attacks.

**Specific Treatment.** (1) *Neonatal Period.*—The commonest cause here is cerebral injury or hæmorrhage. In addition to convulsions, the infant suffering from intracranial hæmorrhage is likely to be flaccid with subsequent rigidity, sucking, respiration and crying are feebly performed. The fontanelle may be bulging, and lumbar puncture will show a blood stained fluid with crenated red cells or a xanthochromic fluid. The infant must be very gently handled and treated for surgical shock. In addition to sedatives, hypertonic saline may be given per rectum. Tube feeding is often necessary. *Asphyxia of the new born*, from whatever cause is liable to result in convulsions. The immediate need of the infant is for oxygen, which should be administered with a face mask or by nasal catheter. 5% CO<sub>2</sub> will stimulate respiration. *Maternal eclampsia* occasionally causes convulsions in the infant. The convulsions are apt to be severe and fatal. *Milk allergy* is a rare phenomenon, the child developing convulsions on being put to the breast for the first time and on each subsequent occasion. *Fresh or dried cow's milk* is taken without difficulty. *Tetany of the new born* is probably a true low-calcium tetany. The infants respond to calcium administration. *Tetanus* may occur when the infection gains entrance by way of the umbilicus, e.g., from use of infected Fuller's earth. Antitoxin should be

given, 2,000 units per 10 lbs. body weight, intravenously and intrathecally.

(2) *Later Infancy*.—The causes are wider and may be broadly classified as follows:

(1) *Infective*:

(a) Infection of C.N.S.—Meningitis, congenital neurosyphilis, etc.

(b) Otitis media and sinus thrombosis.

(c) Infection elsewhere—pneumonia, pyelitis, dysentery, exanthemata.

(2) *Traumatic* and *haemorrhagic*; direct trauma, pertussis paroxysm, etc.

(3) *Metabolic*: tetany, uræmia, hypoglycæmia.

(4) *Toxic*: Metallic and other poisons—e.g., lead, strychnine.

(5) *Congenital cerebral defect* and *progressive degeneration*, microcephaly, amaurotic family idiocy, etc.

(6) Intracranial tumour.

(7) Hydrocephalus.

(8) Peripheral irritation.

(9) "Idiopathic epilepsies."

*Convulsions of metabolic origin* are often associated with rickets and lowered calcium in blood. Calcium therapy, vitamin D, etc. are indicated. *Uræmia* convulsions occasionally occur at the

onset of acute nephritis and as a terminal event in chronic nephritis. An effective method of relief is to give 1 per cent Mg. SO<sub>4</sub> intravenously. This is not without danger and must be done slowly taking blood pressure at same time.

*Peripheral irritation*.—This should be considered last. An acute digestive upset may be sometimes associated with a convulsion. Whether, however, any one of the popular triad of teething, worms, and phimosis is ever really responsible for convulsions is much less certain.

"*Idiopathic epilepsies*." This is an unsatisfactory group. Every effort must be made to control the attacks with drugs, and avoidance of any known precipitating factors; if the attacks persist beyond infancy, they are apt to become more resistant to treatment and associated with a varying degree of mental degeneration.

## ANÆSTHESIA.

### ANÆSTHESIA IN GENERAL PRACTICE.

**Pre-Operative Treatment and Premedication**.—R. MACHRAY, (*B. M. J.*, October 9, 1937, pages 713-715).—The present article outlines the measures that it is desirable to take in the preparation of a patient for operation in so far as these come under the control of the anæsthetist. The extent of preparation necessary or possible will naturally vary widely, but

the guiding principle should be that the patient comes to the theatre in the best possible condition of physical health and mental rest, so that he will the better be able to resist the disturbances that the disease, its operative treatment, and the anæsthetic produce. The period, therefore, between the decision to operate and the operation itself should be utilized with this in mind.

**General Rules**.—The length of time devoted to pre-operative measures will vary with the urgency of the operation. When circumstances allow, it may be advisable for the patient to spend several weeks of easy life, in pleasant surroundings with special attention to diet and sleep. There will be cases in which although the need for operation is urgent, a better result will be obtained if prolonged and complete rest in bed with appropriate medical treatment is enforced. Such conditions may arise from the nature of the disease itself or from some intercurrent affection. It is obviously wise to postpone until better weather operating on patients who are "chesty every winter," and, in general, extremes of temperature and fog should be avoided. Dental sepsis has a definite influence on pulmonary complications. It should, therefore, be eradicated if there is sufficient time for any possible reaction to subside; otherwise such may be done with brushing and mouth washes. These questions are usually outside the

anæsthetist's province, but if the anæsthetist is also the general practitioner they will need consideration.

Coming now to more immediate measures, adequate rest and opportunity for an unhurried preparation are essential, while the early morning, say 8 to 9 o'clock, is the best time for the operation itself. These things can best be arranged for in most instances if the patient enters the nursing home early the previous evening; after a good night's sleep he then has not to wait long for the final preparation before basal narcosis or the anæsthetic itself is begun. In formidable operations and where lengthy preparation is necessary, and in the case of the old and feeble, more time should be allowed and there should be a complete absence of hurrying. Such a course will always be found worth while. In comparatively trivial operations, however, it is permissible for the patient to enter the nursing home only a few hours before the operation, if this takes place in the afternoon.

**Purgation**.—Where no action of the bowels will take place for two or three days, as in abdominal operations, it is obviously desirable that the alimentary canal should be reasonably empty, and in other cases it will usually make the patient more comfortable. But this emptying should be done by the most gentle method possible and vigorous purgation avoided. Many of the drugs employed are mucosal irritants and not only

will produce diarrhoea and a disturbed night but will increase the post-operative discomfort and favour subsequent distension. Another objection is that vigorous purgation will tend to dehydration and acidosis. Frequently the patient will be able to say which aperient and what dose suit him best, and also how long it takes to act; the last is important, as an unbroken night must be assured and the bowels must be opened at least three hours before operation. A suitable purgative is infusion of senna. Sometimes the least disturbing results will be obtained from a combination of mild purgation and an enema. An enema alone will be indicated in two circumstances: first, when there is insufficient time for an aperient to act (although the patient can be instructed to take it at a suitable time before entering the nursing home); secondly, when avertin is to be given. Here success depends so much on complete retention that, unless several hours can elapse after the action from the purgative, it is unwise to risk an irritated bowel and better to rely on a skilfully administered soap and water enema. Even this should be given four hours before the administration of avertin. Pelvic operations need a more elaborate preparations, which is usually dictated by the surgeon.

*Value of Glucose.*—Where dehydration and starvation are present the loss should be made good by giving saline and glucose, by the rectal route if necessary. Pre-operative glucose is valuable in

the prevention of post-anæsthetic acidosis. It should be prescribed especially when there is any evidence of deranged liver function and when previous anæsthetics have been followed by much vomiting. In normal cases it probably has no effect, but since it also has no ill effect it should be given in all cases except the most trivial. Recommended doses vary widely, but probably two or three ounces confer the maximum benefit and should be taken in lemonade with the evening meal. Diabetic patients will need special treatment and a dosage of insulin and glucose, worked out for each case.

*Sleep.*—A good night's sleep is of great importance, and there will not be many patients who can manage this without assistance. A sleepless night will not only cause great mental distress but will be wearing to the patient's physical condition. Even if he has been sleeping well previously it is better to order a sedative. The drug and dose will vary with the temperament, but adequate dosage is essential. Here again, the patient may be able to suggest a drug that suits him or, what is more important, drugs that have no effect or are upsetting. Aspirin and bromides are of help but not certain enough for routine use. Nembutal, gr.  $1\frac{1}{2}$ , is reliable, and may be combined with aspirin, gr. 10. Medinal gr. 5 to  $7\frac{1}{2}$  is more powerful but does not suit everyone. The patient should retire to bed before 10 p.m. and immediately take the sedative, and he

should sleep until about 5 to 6 o'clock. If he wakes early and feels hungry he should be allowed a cup of tea and biscuits. It may be mentioned that should the operation be timed for later in the day light meals can be taken until as late as possible—say, until three hours before. Hunger is bad and starvation may lower the liver glycogen.

Small children will as a rule sleep well with a certain amount of coaxing, but if their surroundings disturb them, and especially if they know they are to have an operation, sleep may be impossible without help. Chloral is a useful sedative in doses of 1 grain for each year of life, with syrup, aurantii 30 minims and water 1 drachm.

*Premedication.*—Several factors need to be considered in deciding what drugs to use for premedication—the temperament of the patient, his general condition, and the anæsthetic it is proposed to employ. The indications for some form of pre-operative sedation fall into two categories. The first is the removal of the unpleasant sensation of being conscious to the theatre and there being anæsthetized with something evil-smelling over the face. Even the placid who seem to approach operations with equanimity may suffer much mental distress, while with nervous patients the removal of this dread may be an important factor in the success of the operation. A pre-operative sedative will also reduce the amount of inhalational anæsthetic requir-

ed, and if suitably selected will make it possible to conduct an operation under nitrous oxide and oxygen when this would otherwise be impossible. It will reduce considerably the amount of ether required in deep anæsthesia for upper abdominal operations. It is necessary, however, to exercise judgment in the selection of cases and in the amount of sedation employed. The action of the drugs used is long and cannot well be reversed once they have been administered. The disadvantages can be summarized as follows:

1. The possibility of the airway becoming obstructed as the jaw relaxes, a condition made less obvious by the quiet respiration, necessitates skilled watching after administration.

2. The depth of narcosis, at first satisfactory, may, if shock develops, become dangerously deep.

3. In such cases insufficient æration may be present afterwards from respiratory depression, although this may have been controlled during the operation. This, too, makes skilled nursing necessary.

4. Such a period of reduced pulmonary ventilation will tend to increase the risk of respiratory complications, while prolonged absence of the cough reflex may have the same risk.

5. The possibility of derangement of liver function by barbi-

turates, and possibly by avertin, in cases of hepatic insufficiency.

Unless he has some experience in pre-operative medication the anaesthetist would do well to keep within the recognised scale of doses—or below, when age, weight, or feebleness suggest caution. In any event sedation should not be pushed to the stage of full anaesthesia (evipan and pentothal are not now being considered), but this should be completed by some inhalational method more under minute-to-minute control. Some obstetricians consider it unwise to give anything but atropine before Cæsarean section because of the depressing action on the foetal respiratory centre.

**Atropine.**—The most commonly used drug is atropine. It decreases the secretion of mucus and paralyses the vagus, thus diminishing one of the dangers of chloroform. It has no sedative action. For patients over the age of 2 years the dose is grain 1/100. Below this age it should be prescribed as follows: up to 6 months grain 1/300; 6 to 12 months grain 1/200; 1 to 2 years grain 1/150. Atropine should be given in all cases except in operations of only a few minutes' duration and in those in which hyoscine is being used (hyoscine has a similar action to atropine in reducing secretion). Hyoscine is better substituted for atropine in cases of hyperthyroidism in view of the metabolic stimulation of atropine.

**Morphine and Hyoscine.**—Pre-operative sedatives fall into two categories; those producing drowsiness and amnesia, and those producing unconsciousness. The first category is represented by morphine and hyoscine, which together form an extremely good combination. The standard dose for adults is: morphine grain 1/6 to 1/4; hyoscine grain 1/150. In some cases the patients will be asleep when the anaesthetic is started, but short of this there will be drowsiness and absence of anxiety and afterwards a partial or complete amnesia. Omnopon gives rather better results than morphine; the usual dose—grain 1/3—is the equivalent of rather more than 1/6 grain of morphine.

There are few contraindications but some drawbacks. In view of the respiratory depression—not great, however, and usually more noticeable during the anaesthetic than before—pure chloroform should not be used and avertin is better avoided. For the same reason open ether is sometimes more difficult to give. The shallow breathing and tendency to apnoea make it difficult for a sufficient quantity of anaesthetic to be introduced. The signs of anaesthesia are less obvious and the anaesthetist may be misled by a condition similar to chloroform sleep. But with experience this can be overcome. Carbon dioxide is a valuable help. These objections apply to all pre-operative sedation and make the use of some form of closed anaesthesia with its greater control of respiration desirable.

Morphine and hyoscine are safe, and will be found the most suitable agents for routine use before general and spinal anaesthesia. The doses recommended here are as a rule sufficient, but may be exceeded in suitable cases. The injection should be given one hour before the operation and preferably with the patient on the stretcher or trolley. The room should be darkened and kept quiet, as with all forms of sedation. The action of morphine and hyoscine may be supplemented by an intravenous injection of one of the short-acting barbiturates—evipan or pentothal—which should be given immediately before induction of the inhalational anaesthetic and should be pushed to the stage of profound sleepiness just short of surgical anaesthesia. When either of these two drugs is to be used as the main anaesthesia, a similar injection of morphine and hyoscine will be found to improve the anaesthesia and reduce the dosage.

**Basal Hypnosis.**—Paraldehyde is the safest basal hypnotic. In normal doses it does not depress respiration and the cough reflex is not abolished. Since it is excreted in the breath it has no effect on liver or kidneys. Its smell is noticed least by the patient. It is administered in ten times its bulk of saline as a rectal injection with the patient on the left side. The standard dose is 1 drachm per stone of body weight and should be given one hour before the operation. Young children, the elderly, and the sick should receive about 20 per cent

less. Results are good but consciousness is not always lost, although there will be no recollection of this.

Avertin is the most reliable in its hypnotic action. Its dosage (0.1 gramme per kilogramme of body weight) and method of preparation can be obtained from a table supplied by the makers and should be adhered to. Obese and elderly patients require a smaller dose—say, three-quarters—while the maximum should be 8 grammes. In cases of doubt it is best to run in three-quarters of the selected dose and after a quarter of an hour to use the remainder if consciousness has not been lost. It should be given half an hour before operation and the patient be kept on the side until the anaesthetic is started. This will minimise the risk of obstruction as the jaw relaxes.

## ENDOCRINOLOGY

**Action of Testosterone Propionate on the Female—Clinical Applications and Dosage.**—GEORGE L. FOSS, (*Lancet*, pp. 992, dated 30th April 1938).—In experiments on rhesus monkeys Zuckerman (1937) found that inhibition of follicular maturation and luteinisation with consequent suppression of the menses followed administration of 25 mg. of testosterone propionate twice weekly during a period of seven months. Cotte, Motrin, and Mankiewicz (1937) have reported similar results in the rabbit, and Robson (1936 and 1937) has shown that in rodents simul-

taneous administration of testosterone and oestrone prevents oestrus.

The natural outcome of this experimental work has been the use of testosterone as a remedy for excessive and irregular uterine bleeding due to hyperfolliculinæmia in the human female, especially as Zuckerman's work was fairly conclusive that it caused no undesirable secondary effects, except perhaps enlargement of the clitoris.

Loeser (1938a) began using testosterone propionate for gynaecological conditions in April 1937, and the author has used it since July 1937. Several papers have appeared already on its employment for painful breast conditions, chronic, cystic, mastitis and premenstrual mastodynia, also for dysmenorrhœa (Desmarest and Capitain 1937 and 1938, Goormaghtigh 1938, Turpault 1937, Bender 1937). The author's early results in gynaecological disorders were variable, probably because my doses were not always adequate. Experiments with a eunuch (Foss 1937b) and observations made about the same time by Hamilton (1937) in America suggested that doses of 40 mg. per week probably would be sufficient. The first case supported this belief:

*Case Records.*—*Case 1.* Mrs. A., aged 45, with severe metrorrhagia, was awaiting hysterectomy; her condition was very poor with severe anæmia, dyspnoea, and lack of energy. Seen on July 18th she was given 40 mg. of testosterone propionate twice weekly in five doses. Five days after the last injection curettage showed that the endometrium was in the resting stage. Three days later scanty bleeding started, lasting

six days, six diapers only being soiled. Immediately, a second dose of 200 mg. in five injections was given during fifteen days. Curettage on the twentieth day showed resting-stage endometrium which was difficult to obtain by the Sharman and Sheehan (1937) and Foss (1937a) curettes. On the twenty-seventh day no endometrium at all was procured. From the twelfth to the thirty-fifth day of the cycle there was scanty brown staining, but after this no further bleeding was seen until Jan. 1st to 8th, 1938; it was scanty and entailed the use of twelve diapers. During the period of twenty weeks' amenorrhœa, she was troubled with hot flushes and sweats which were readily controlled by oestrone dragees. One other very scanty period only has been since then (Feb. 18th, 19th) using four diapers. So far this patient has been saved from hysterectomy, and her general condition improved very rapidly once the flooding stopped.

*Case 2.* Miss B., aged 25, who had menorrhagia and dysmenorrhœa, was given 140 mg., 200 mg., and 150 mg. in three consecutive days without any effect on the loss or on the length of the cycles. Later she was given 500 mg., again without altering the duration of the cycle, but the loss was not quite so excessive and dysmenorrhœa was still slight.

*Case 3.* Mrs. C., aged 48, was seen in September last. She gave a history of continuous bleeding for 2½ months without stopping. Before this she has had very severe floodings in November, 1936, and January 1937, lasting three weeks; she also gave a history of many years' menorrhagia with flooding and passage of clots. Injections of testosterone propionate were given and after 270 mg. had been injected in nineteen days the bleeding stopped. Amenorrhœa persisted for sixty-three days; then she had a fairly heavy period lasting eleven days. Since December 22nd she has been amenorrhœic. Curettage a week after the last injection showed endometrium with small early-interval-type glands.

Cases of longer standing, however, seem to require very much larger doses.

*Case 4.*—Mrs. D., aged 40, a very obese woman with a history of severe menorrhagia, had a continuous hæmorrhage from February 1937, until she was curetted on July 12th when her endometrium was found to show some hyperplasia. The loss was very excessive all the time and she

used three or four diapers daily, changing even during the night. After curettage, bleeding continued for three weeks and then she had a clear week. Injections of testosterone were started on September 29th; after 250 mg. bleeding began in three days and was almost as copious as before, but the interval had increased. Rhythmic treatment was given now for the next five months. The only result was to re-establish monthly cycles once more, and there was not much effect on the loss. Dosage was therefore increased and after 500 mg. had been given in three weeks, bleeding was more normal lasting only six days instead of ten to fourteen, and there was no flooding or clots. An interesting fact was noticed now—she complained of numerous hot flushes and sweats both by day and night. After the last bleeding the dosage was increased to 200 mg. weekly and the menopausal symptoms have become much worse, as many as ten to twenty flushes daily being counted.

This moderately severe case has shown how variable the effective dosage is. A still more refractory case has been treated and has been a failure so far, after very great dosage.

*Case 5.*—Miss E., aged 30, a nurse, had pneumonia in 1936. Previously her periods had been regular (every 28 days and lasting 5 to 7 days). A fortnight after her illness, bleeding started with variation in flow and an occasional clear day, and she had been bleeding for fifteen months. Medical treatment had failed and in April 1937 she was curetted; the endometrium showed hyperplasia. No benefit at all was obtained. Starting on October 1st, 340 mg. of testosterone propionate was given in three weeks, with perhaps some slight diminution in loss and with more frequent days of rest. The losses persisted, however, and owing to the nature of her occupation, treatment was not always available. She was admitted to hospital again in March 1938, and examined under anæsthesia; the uterus was small. An intensive course of testosterone propionate was started on March 14th and she was given 100 mg. daily. After 800 mg. bleeding stopped for four days, but it then started once more just as badly. After 2000 mg. bleeding still persists and treatment is being continued.

For a case of metrostaxis in a girl of 18 testosterone proved of great value.

*Case 6.*—Miss F., aged 18, started periods at 15; it was followed by two scanty periods and then three months' amenorrhœa, after which she had hæmorrhage lasting four months. Dilatation and curettage on July 20th, 1935, showed glandulocystic hyperplasia and she was treated with a small dose of radium. Amenorrhœa persisted for a year, followed by alternating periods of flooding and short rests. During this time she had been treated with copious luteum, sistomensin, and prolamin by mouth. When seen on January 24th, 1938, she had been bleeding almost continuously for twelve months and was in poor health. The loss varied and she wore a diaper continuously. She had about two days clear and then bleeding would start again in gushes. Injections of 20, 40 and 50 mg. of testosterone propionate were given twice weekly and afterwards the dose was increased to 100 mg. After 510 mg. in twenty-five days, bleeding stopped completely. This was followed by a slight discharge, but after a further 200 mg. she left off all diapers. Five weeks after the last injection she had had on suspicion of return of bleeding. She has regained her energy and her general health has improved. A normal five-day period started on April 3rd after six weeks' amenorrhœa.

It appears from experience of about 16 cases that for most patients total doses of 500 to 800 mg. are required, according to the severity and duration of bleeding and the nature of the disorder to inhibit endometrial proliferation. In some cases of menorrhagia cyclical doses of 20 to 40 mg. given twice weekly for a few months are sufficient to counteract follicular overaction, or to restore a cyclical rhythm in metrorrhagia. Severe cases need a total dose of 800—2000 mg. given in daily injections of 100 mg. or twice weekly injections of 150 to 200 mg., the individual dosage being adjusted to the clinical history.

The successful results of Loeser (1938a and b) were obtained with very similar dosage.

*Discussion.*—Why testosterone propionate should have an action so antagonistic to that of oestradiol is not known. Chemically testosterone is a very close relation to oestradiol and it can be made synthetically by complete hydrogenation of dihydroxy-oestrin or oestradiol. It is known that administration of testosterone propionate in a male gives rise to excretion of both androgen and oestrogen in the urine. This was shown originally by Steinach, Kun, and Peczenik (1936) on rats and later in humans (Steinach and Kun 1937) and has been demonstrated several times by Callow (1938). Urine analysis, kindly carried out by Callow, of a eunuch under treatment with testosterone propionate, showed that there was a parallel increase in output of androgen and oestrogen during administration, in the ratio of 1.6 to 1. After five weeks' rest from therapy this ratio was 3.88 to 1, whereas in the normal male urine the ratio was 1.71 to 1.

The fact remains that experimental and clinical work has proved that testosterone propionate injected into females counteracts the natural follicular hormone. Two possibilities suggest themselves: (a) that the male hormone is a direct antagonist of the follicular hormone, and (b) that it inhibits anterior pituitary gonadotropic hormone. The second is perhaps the more likely hypothesis, as shown by inhibition of follicular maturation in the rhesus monkey.

Quantitative assays for gonadotropic hormone in the urine from a eunuch (Foss 1938), while at rest and also while under high dosage of male hormone, might shed some light on this matter, but unfortunately the results are not yet available. Clinically, Salmon (1937) found that testosterone propionate gave relief from menopausal symptoms in an ovariectomised woman and also reduced the amount of gonadotropic hormone recoverable from her urine. Further assays on the urine of menopausal women, before and after male-hormone therapy, will be awaited with interest.

Before testosterone propionate can be regarded as a valuable addition to gynaecological practice, it is essential to study its effects in very large doses over a long period. In a comparatively small series of 16 cases during the last nine months, doses up to 2200 mg. have been given in periods ranging from three to twenty-eight weeks, and in all this series no unpleasant side effects have been noticed. These doses are smaller proportionately than were given by Zuckerman (1937) to monkeys weighing 11 lbs and he was unable to find any abnormal or harmful effect beyond enlargement of the clitoris. In patients receiving intensive therapy for a short time or moderate doses over a long period, there was definite increase in size of the clitoris. I do not regard this as an unpleasant effect however, for no patient complained of discomfort or swelling of the genitalia, and in each case it had to be looked for. In

some, clitoris was about  $\frac{3}{4}$  in. long and  $\frac{1}{4}$  in. across at the base. Whether its size decreases again when administration of hormone ceases is not yet known.

Loeser (1935b) in one case noticed some voice change to the gruff male type after 1500 to 2000 mg. but the voice soon returned to normal on discontinuing treatment. It was doubtful whether this was due to the therapy.

The amenorrhoea induced by testosterone propionate is also of fairly short duration and restitution of previous normal rhythm takes place when injections are finished. In most cases the endometrium is in the resting stage and the glands are of the interval type; in no case has a secretory-phase endometrium been found. Many reports, already referred to, have appeared on the use of testosterone for mastopathia and mastodynia. During treatment the breasts decrease in size, and this may have a useful application for macromastia of endocrine origin.

*Case 7.*—Miss G., aged 22, was a medical student with mastitis. She had had a serious and sometimes blood-stained nipple discharge for eight months. She was given 270 mg. testosterone propionate in a month. Menstruation was not inhibited but its onset was unexpected and sudden on two occasions, owing to the absence of premenstrual mammary congestion and fullness, malaise, and backache. The discharge gradually became more sticky and eventually stopped. During this time both breasts diminished in size—a fact reported both by her mother and herself—but as yet there has been no appreciable alteration in its lobulated condition.

From the author's experience in over 40 cases of males and females

treated with testosterone propionate, it appears that in the absence of oestrogen in the body—for example in eunuchs—small doses of male hormone suffice. To obtain a similar effect when testicles are present requires very much larger doses possibly because of the breakdown of endogenous testosterone to oestrogen, especially in old age. In females the dose of testosterone must be much greater still, since higher levels of oestrogen are encountered, especially in conditions such as metropathia hæmorrhagica. The finding of Zuckerman (1936) that a testosterone-oestrone ratio of 7 to 1 is necessary to inhibit the action of oestrone on the immature rhesus monkey's prostate applies to human dosage. Experimentally, endometrial glandulocystic hyperplasia can be produced with doses of 50 to 100 mg. of oestradiol benzoate. Accordingly to treat severe cases of this condition due to endocrine dysfunction 350 to 1000 mg. would probably be an average dose.

**Cutaneous Application of Follicular Hormone.** B. ZONDEK (*Lancet*, May 14, 1938).—The oestrogenic hormone is absorbed through the skin, but if it is applied in an oil or ointment the dose needed to produce oestrus in castrated mice is seven times as great as the dose needed when it is injected subcutaneously.

If the hormone is dissolved in benzol, ether or 96 per cent alcohol, it is much more readily absorbed through the skin.

A dose of oestrogenic hormone given in this way is just as effective as the same dose injected subcutaneously.

The equal effectiveness of percutaneous application in a suitable solvent has been shown by experiments in which oestrogenic hormone was used to produce oestrus in mice, to reduce the growth of the testes of rats, to inhibit the growth of young rats and to produce a pituitary tumour in the rat.

In gynaecological practice injections of oestrogenic hormone can be partly replaced by percutaneous applications of alcoholic tincture of oestrone. Progesterone also is absorbed by the skin, but it will have to be injected until it is less expensive, for larger doses are required for percutaneous than subcutaneous administration.

Application of oestrogenic hormone to the skin, followed by the injection of progesterone, will produce uterine bleeding in primary and secondary amenorrhoea.

The rubbing of alcoholic tincture of oestrogenic hormone into the skin is almost as effective clinically as injections of the hormone but some patients who do not react to percutaneous treatment will nevertheless react to injections.

### VITAMINS.

**Vitamin A.** BESSEY AND WOLBACH (*J. A. M. A.*, June

18th, 1938 **Vitamin A and the perception of light.**

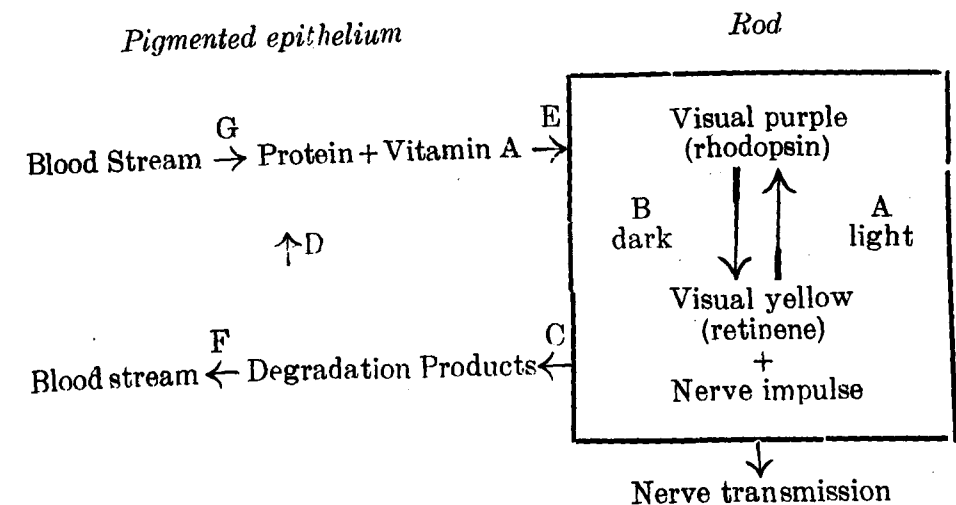
*Vitamin A and cell physiology.*—One of the earliest functional changes observable in association with vitamin A deficiency is a decreased ability for dark adaptation, nutritional night blindness which responds to vitamin A therapy. The quantity of visual purple present in the retinas which have been dark adapted for varying periods demonstrates that the resynthesis of visual purple in vitamin A deficient animals is abnormally slow. It is possible also to demonstrate experimentally the correlation between the slow rate of degeneration of visual purple and the delayed dark adaptation. Faulty twilight vision in vertebrates occurs with vitamin A deficiency because the mechanism for the formation of visual purple in the rod of the retina is defective.

Wald has recently shown the previously reported high vitamin value of retinal tissue to be due to vitamin A. He has presented strong evidence that visual purple is a conjugated protein in which vitamin A is a prosthetic group.

The cones of the retina are associated with the perceptions of colour and other visual functions which depend on light of high intensity, while the rods are sensitive only to light and are especially adapted to function in dim light.

The outside end of the rod which lies adjacent to the pigmented epithelium of the retina contains visual purple (rhodopsin) found only in the rods and serving to transform the energy of dim light into nerve impulses which vary, within limits, with the intensity of the light. Although

the complete details of this photochemical process have not been ascertained, it has been suggested and considerable proof obtained that the cycle of events in the retinal rod when a molecule of visual purple receives a quantum of light energy is that shown in the accompanying illustration:



The photosensitive pigment (visual purple) absorbs the light and as a consequence is decomposed into products which initiate a nerve impulse (reaction A). Other chemical systems immediately intervene to resynthesise these products to a new molecule of receptor pigment (reaction B or C+D+E) or they are disposed of as waste materials (reaction F) and an entirely new molecule is made from fresh raw materials to take their place (reaction G+E). The quantity of visual purple which is present at any instant will depend on the difference between the rate of decomposition (reaction A; intensity of light) and the rate of

synthesis (reactions B and E). In bright light the equilibrium of these reactions is displaced so that visual purple is practically absent from the retina, while in the dark the equilibrium is displaced in the opposite direction and visual purple is present in maximum quantity. Normal vision in dim light, whatever may be the details of the reaction, depends on an equilibrium somewhere between these two extremes.

Two processes are proposed for the synthesis of visual purple: from visual yellow by simple reversal of photolysis and from the protein plus vitamin A with

aid of the pigmented epithelium. That a certain proportion of visual yellow or retinene is converted into visual purple is observed in the isolated retina which has been bleached and replaced in the dark; the remainder decomposes and is lost or resynthesised by aid of the pigmented epithelium.

The latter process takes place in the intact eye but has never been observed in the isolated retina. In vitamin A deficiency reaction B or E are both too slow to keep the supply of visual purple adequate.

The fact that pigmented epithelium is essential to the visual purple process suggests the possibility that it, like other epithelial structures in times of vitamin A scarcity, may not function normally and thus indirectly also contribute toward visual impairment.

The chemistry and physiology of vitamin A as revealed in its function as a component of visual purple do not necessarily imply the presence of a photosensitive substance in the more generally affected epithelial cells. However, they do suggest that vitamin A may serve as a prosthetic group in other conjugated proteins. The exact nature of these substances and how they function is one of the most interesting problems in cell physiology.

**Less Well-known Vitamins.**  
C. M. MCCAY (J. A. M. A., Vol.

110, No. 18, 30th April 1938, pp. 1441).—Under the title of 'Other Factors' one can include only a few of the many essential organic substances that various animal species seem unable to synthesize. The description of these substances is scattered throughout the vast literature of biology. Many more have probably been missed than have been found. Such substances may seem of little importance at this time, but who can say when the needs of some insect with specific requirements may provide the key for studying the vitamin physiology of higher species? These ramifications of nutrition are well illustrated by the discovery of Trager and co-workers that a factor essential for the growth of mosquito larvae is present in normal human urine but deficient in that of pernicious anaemia patients.

To appreciate the expanse of unexplored fields in the domain of nutrition, one need merely read some modern work such as "Culture Methods for Invertebrate Animals" by Needham. All recent tests with insects indicate that they require special factors that have not been described thus far as essential for higher forms. To-day one can only postulate that, as higher forms such as man lost their fine and acquired hands in the course of evolution, they also abandoned some of their primitive vitamin needs and acquired still others.

Crowell and MacCay found that even clothes moths require

some of the fractions of yeast. No clear-cut evidence has ever appeared, on the other hand, which indicates that any insect species requires either vitamin A or D, although certain lipid materials, possibly sterols, seem essential to such forms as the cockroach.

Trager, in discussing the nutrition of mosquito larvae, concluded that there must be certain compounds other than the recognized vitamins that are essential. Frost and others found that mosquito larvae need certain essentials in yeast but not vitamin A, B, C, D, or E. Fortunately, students of insect nutrition have attempted to label their discoveries with letter and subscripts. Such consideration for the future of the science of nutrition, however, must not be rewarded by neglect of their discoveries.

If one considers still lower forms than insects, one must enter the fields of bacterial nutrition, where other parts of the alphabet, such as V and X, have been used to describe specific factors. Knight has provided an excellent summary of the nutrition of bacteria with considerable space devoted to vitamin factors.

The minute amount of growth stimulants with which the nutrition student of the future will have to be concerned is suggested in the recent studies of Kogl, who has isolated a factor from yeast which acts in a concentration of one part in four hundred billion.

**Factor H.**—The lower vertebrates, with the exception of fish, have been given little attention by students of nutrition. For the past period of nearly a century during which trout have been domesticated, it has been known that the various species require some factor present in fresh meat. After a series of studies in which trout were fed synthetic diets of purified constituents supplemented with yeast, tomato juice and cod liver oil, McCay, Bing, and Dilley found that trout could not live unless fed a small amount of fresh meat. This component was termed "Factor H." In a series of later studies it was found to be thermolabile and readily destroyed in the course of ordinary drying. However, part of it was preserved when such sources as liver were dried in vacuo in inert gas. This substance is present in all fresh body tissues that have been studied. It seems to be the dominant factor in the nutrition of trout. The literature concerning this factor has been reviewed recently. This factor seems to be essential for carnivorous species such as the fox.

The letter H has also been applied to a totally different substance, which Bocher finds essential for rats. This factor is said to be heat stable but destroyed by alkali. She finds it essential for growth of the rat.

The term "vitamin H" has also been used at times by Paul Gyorgy to describe one of the fractions concerned in rat dermatitis. A recent German work

has included an entire section under the heading of "Vitamin H." In this summary Stepp and his co-authors define H as the dialysable, heat stable substance which is set free from liver proteins by digestion and proteolytic enzymes, according to the observations of Gyorgy. They assume that this essential is needed by the rat, the chicken and man. There seems little justification for including all these diverse discoveries under this common name. Furthermore one wonders why the term H should be used to describe the growth factor of Williams, Lewis or Hunt. Apparently, the Germans are already marketing some preparations supposed to be concentrates of this factor under the names "Huco Salve" and "Murmil."

#### *Miscellaneous Growth Factors.*

—The literature dealing with lower forms of life teems with unnamed and ill defined vitamins. There are fewer such factors described for the vertebrates that are popular with orthodox students of nutrition: namely, the rat and the chicken

The growth factor for chicks described by Arnold and his associates has proved to be the amino acid arginine, thus accounting for the growth stimulation by such products as peanut meal, liver residue and soya bean meal.

In 1931 Guha found that there were certain factors in milk, grass, spinach and egg yolk that stimulated the growth of rats fed

B fractions in the form of vitamin B-1 and autoclaved marmite. To preserve these fractions he found it essential to dry the products at 35° C in front of a fan. The potency of these materials was lost in both fractions through extraction with ether.

Hogan and his co-workers have shown the need of herbivorous species for some factor that is present in plant juice or alfalfa. During the past two years, evidence has also accumulated in the Animal Nutrition Laboratory at Cornell that lambs require some factor, other than the recognised vitamins, that is present in freshly sprouted oats. Kohlet and his co-workers noted the growth stimulating properties of grass juice.

In 1929 Coward and her associates found that some factor was contained in certain preparations of casein and was deficient in others. When a particular sample of casein proved deficient it could be supplemented satisfactorily by milk, lettuce, liver or wheat embryo. These studies were made with rats in the course of other assays.

Liver has provided a fertile source of growth stimulants. It has long been recognized that the essential constituent for brook trout, factor H, is richest in beef liver. The past ten years has indicated that liver has several essential factors, and there is little doubt that many will be discovered as new species are considered by students of nutri-

In 1932 Mapson postulated the existence of a growth factor in liver. It was soluble in 90 per cent alcohol and also in water after the liver was subjected to digestion with papain. This factor was called "physin". Seegers and his co-workers also found that liver contained a growth factor. This tended to be lost on heating. Liver heated at 100° C. for two weeks lost this capacity to stimulate the growth of rats, although the biologic value remained unchanged as far as the protein was considered.

Elvehjem and his associates have postulated several new factors. Among them is included one for stimulating the growth of rats. They found this in the alcohol ether precipitate from water extract of hog's liver. They find this is heat labile, so it falls among the thermolabile B factors and needs no further discussion here, other than to note it with the other factors of liver. This factor has recently been christened W by Frost and Elvehjem.

Halliday and Evans attempted to confirm these observations of Elvehjem and his co-workers but came to the conclusion that the precipitate from hog's liver was carrying down Vitamin B-6. Therefore they decided that there was inadequate evidence to postulate such a new factor.

The "Y factor" described by Chick and Copping also is found in liver as well as in yeast and its water extracts. This factor is one of the B fractions needed for

growth by the rat. Its nature is gradually becoming clear in the course of such thorough studies as those of Edgar and Macrae. These authors find another factor adsorbed on fullers' earth which is neither vitamin B-6 nor riboflavin.

Among the liver extracts must also be included the filtrate factor of Lepkovsky and Jukes, which seems potent in curing dermatitis in chicks, black tongue in dogs and pellagra in man. This may be identical with the "Y factor", already described, and nicotinic acid.

In order to rear chickens on synthetic diets, Hogan and his co-workers had to supplement the basal diet with wheat germ oil, acid hydrolyzed yeast, and liver extract in addition to carotene and irradiated ergosterol. One can only speculate concerning the undiscovered factors in such an array of supplements.

In 1928 Hunt discovered that there were at least three factors in yeast that were essential for the growth of the rat.

In the course of growth studies with rats, Williams and Lewis also found a factor left in yeast residues after extraction with water and alcohol. This growth factor could not be extracted with any solvent. No later work indicates its relations to the new B fractions.

Vitamin I, or B-7, is the factor postulated by Centanni. He

found that an alcohol extract of rice polishings prevented digestive disturbances in pigeons but did not prevent the symptoms of polyneuritis. Methyl alcohol was the best solvent among the alcohols. Ethyl alcohol was effective at from 95 to 100 per cent but extracted only part of this factor at a 70 per cent concentration.

This I factor recalls the claim of Rosedale made ten years ago. At that time he precipitated the water extract of rice polishings with lead acetate and carried down a factor that permitted evacuation of the bowels and checked the constipation associated with polyneuritis in birds.

This also recalls the factor of Carter. He found that the heart rate slowed down when pigeons were fed polished rice but that recovery was much slower from feeding B-1 than from such feedstuffs as yeast and wheat. All these factors are difficult to evaluate, since polished rice is such an unbalanced diet in many respects.

Factor J is the term applied by von Euler and Malmberg to a substance found in fruit, especially St. John's berries. This factor seems to cure pneumonia in guinea pigs, while cevitamic acid will not.

*Vitamin K and other Blood Clotting factors.*—Vitamin K is a specific fat soluble substance the absence of which in the diet of

chickens causes the blood to become very slow in clotting. Thus far no evidence has indicated its importance for other species, although attempts to study the requirements of other species have been very limited.

The observations that led to this discovery were made by Dam while attempting to determine whether hens could synthesize cholesterol. At this time he was feeding a synthetic diet composed of casein, starch, salt, marmite, filter paper and cod liver oil. In earlier studies, using a similar diet, he had observed subcutaneous and intramuscular hemorrhages as well as erosion of the gizzard. He had also noted that these chickens were anæmic and that the number of erythrocytes was only about two million instead of three or more. In 1930 Horvath also observed that the coagulation of the blood of chickens was accelerated by diets of sprouted soya beans.

The same hæmorrhagic condition described by Dam was reported by McFarlane and his associates in 1931 when they were attempting to establish the need of chickens for fat soluble vitamins. These workers were employing diets of about 70 per cent rice and 15 per cent marmite supplemented with various protein sources such as fish meal and casein. They suffered heavy losses from hæmorrhage in chickens fed on a diet containing either extracted fish meal but no losses if the fish meal was

not extracted. Further, they found that blood from chickens fed this extracted fish meal could set in the laboratory over night without clotting.

In 1934 Dam and Schonheyder found that this disease, which resembled scurvy in some respects, developed while the fats from rye, sunflower, corn and rice had no effect. Cod liver oil was also without effect.

Dam and his co-workers later found that the normal amount of prothrombin was lacking in chickens fed a diet deficient in vitamin K. The condition could be developed in about three weeks on a diet of casein 10, ether extracted pig's liver 10, dried yeast 15, sucrose 62.3, salt mixture 2.7, and cod liver oil 4. Three days after vitamin K is fed to deficient animals the blood becomes normal.

Rats and guinea pigs were fed a diet similar to that used for the chickens but no symptoms developed. A man suffering from hemophilia also yielded no response to the feeding of concentrates of the vitamin.

The factor was concentrated by Almquist in 1936 so that 2 mg. formed a sufficient supplement for 1 kg. of feed. This concentrate was prepared from a hexane extract of alfalfa. By distillation this material was concentrated still further. Under very low pressure the potent material could be distilled at from 120 to 140 C. This vitamin is unstable

to alcoholic alkali and is unsaturated as well as colourless. It has no sulphur or phosphorus but a small amount of nitrogen. Colour tests indicate an indole nucleus.

This vitamin seems to be, synthesized by bacterial action since its amount tends to increase in foodstuffs subjected to such action. The amount also increases in the fæces of chicks on the deficient diet if these stand for a day. The diet of the hen may also influence the development of the disease in chicks.

About 1931, claims were made that vitamin A was concerned with the clotting of blood. As purer preparations became available, however, this was disproved. Recently, however, Schiff and Hirschberger have found that there is some factor, which they term T, in egg yolk and sesame oil. This seems to increase the platelet count in both human and rat blood. They found that from five to ten drops of sesame oil per day of five egg yolks affords ample of this essential for treating children. It has also been claimed that semi fasting dogs develop a severe thrombopenia and need this essential. Evidence is not clear that factor T and vitamin K are related.

The failure of blood to coagulate in "sweet clover disease" has long been recognized, especially in young cattle that have consumed partly spoiled clover. Quick finds that this disease can be reproduced in rabbits. It is

cured by feeding alfalfa. However, this disease is not related to the vitamin other than that alfalfa probably acts in furnishing materials for the synthesis of prothrombin. Hogan also observed that the ether extract of alfalfa prevented the hæmorrhages of the nursing young in the case of rabbits.

It is well known that some fish meals are injurious to animals. Scott and Cook find that this injury is due both to the deficiency of vitamin K and to toxic factors in the fish meal. The toxic factor is chiefly reflected in the distorted blood picture with marked increase in lymphocytes and leukocytes.

*Vitamin P.*—Vitamin P is the term applied by Rusznyak and Szent-Gyorgyi to a substance that occurs in lemon juice and red pepper. In certain pathologic conditions characterised by increased permeability of the capillary wall, they found injection of concentrates to be effective when cevitamic acid failed. The early work indicated that the effective agent belonged to the vegetable dyes of the flavine group.

Workers from the same laboratory used guinea pigs that were fed a diet to produce scurvy. They found that these animals finally died of scurvy if fed the concentrate of vitamin P termed "citric." However, these animals lived for about forty-four days, while the others lived only twenty-eight days.

The existence of this "vitamin P" has been questioned by Zilza. The present evidence as far as the experiments on guinea pigs are concerned, indicates that there is no reason for postulating a new factor. His work seems to show that the animals were suffering from vitamin C deficiency, which was relieved to a slight extent by contamination of the "citric."

*Nicotinic Acid.*—From time to time nicotinic acid returns among the growth stimulants that resemble vitamins. Thus the Funks have presented evidence recently that the growth of rats and pigeons is stimulated by such derivatives. This work is interesting in the light of the need of staphylococcus for the same essential as a supplement to B-1 as reviewed by Kogl. Furthermore Elvehjem and his co-workers have found that nicotinic acid will cure black tongue in dogs. These workers have isolated considerable amounts of crystalline nicotine amide from active liver fractions. The effectiveness of this compound in the treatment of human pellagra has now been established.

*Toxic Substances.*—The specific toxicity of various foodstuffs and the counter action of other vitamin-like components of the diet cannot be neglected in a discussion of vitamins, although the subject material is too extensive for detailed consideration here. Throughout the literature on nutrition one is confronted from time to time with reports of toxicities from natural feedstuffs.

especially when they are fed in certain mixtures. A few of the products that can be recalled readily are linseed meal, cottonseed meal, wheat, corn, oats, clover, fish, fish liver oils and egg white. Even in the case of such a familiar product as linseed meal, in which the evidence is quite clear that a glucoside is the toxic agent, one who reviews the literature critically is aware of the many discrepancies involved. When one undertakes to analyze the various factors that interplay to protect or poison an animal with the cyanides from such products, the problem becomes more complex.

In recent years definite advances have been made in studying the neutralization of food toxins by vitamin-like substances in only a few cases.

In 1916, Bateman noted the toxicity of large amounts of egg white and the loss of this property after heating, acid denaturation and proteolytic digestion, according to Stepp and his associates. In 1927 Boas found that rats suffered from dermatitis when the protein of the diet was supplied by certain forms of dried egg white. However, she learned that this disease could be cured if the wheat starch in the diet was replaced by potato starch. At the end of her first study she was uncertain whether she was dealing with a vitamin deficiency or a toxicity. Later she seemed to lean to a toxicity theory.

Parsons and her associates have given special attention to this

problem in recent years. They find that the toxicity of dried but uncoagulated egg white is rendered innocuous either by cooking as observed by Boas, or by feeding substances such as dried yeast or dried liver. Furthermore, these workers report that the neutralizing factor is found in the organs of different species in different amounts. Human liver varies in its concentration of the factor while turkey liver is very rich.

The toxicity of fish liver oils is another field that has been studied during the past ten years. The ability of alfalfa to counteract partly this toxic property was recognized by Woodward and McCay. However, no diet was devised that would do more than delay the development of the degenerative changes. Later Madsen found that cottonseed oil would partly counteract this toxic factor of cod liver oil. Even in rats Norris and Church found that yeast and cod liver oil interplayed in the diet. Instead of a sparing action on the B requirements by the fat of cod liver oil, they found that they must increase these B factors to obtain normal growth. This finding is especially interesting, since the rat is so immune to most food toxins compared to such species as guinea pigs. Recently Yamamoto extended this study of the interplay between yeast and the toxic factors of cod liver oil.

This toxic factor of cod liver oil in the case of herbivora is shown in two ways; first, in de-

generative changes in tissues and, second, in lowering the secretion of the milk fat by a lactating cow. Limited evidence indicates that the toxic factor is the same in the two cases, according to the observations of McCay and Maynard. This factor is found in the saponifiable fraction and is probably an unsaturated compound, since hydrogenation of cod liver oil causes it to lose this toxic action. No explanation has been offered concerning the method by which such substances as alfalfa and yeast can react with an unsaturated fatty acid to remove its toxic action.

Hilditch and Thompson have produced evidence indicating that the unsaturated fatty acids of the C20—C22 series may amount for part of the toxic action of cod liver oil. This is probably only part of the explanation, however, because salmon oil, which is rich in these same compounds, fails to produce the consistent effect of cod liver oil in lowering the secretion of milk fat. No mechanism has been devised to explain the interplay

between dietary constituents in the case of either of poisoning from egg white or of that from cod liver oil.

Finally a third field that has been given considerable attention in recent years is that concerned with the cerebellar disorder in chicks first discovered by Pappenheimer and Goettsch. The food this to be produced in chicks fed a diet of milk powder, casein, starch, yeast, cod liver oil, salts and filter paper. In ducks fed a similar diet, injury to the muscles developed with no effect on the brain, an observation of special interest because it shows that a science of nutrition cannot be grounded on one or two species such as the rat and the chicken. In later studies, vegetable oils, incorporated in the diet at 20 per cent levels, were found to afford complete protection in the case of chicks. Jungherr and Pappenheimer have found more recently that turkeys respond to this diet in a still different manner. The species develops selective necrosis of the smooth muscle of the gizzard wall.

### ODE TO BITTERNESS.

According to the Freudians (but *not* prosaic surgeons),  
Unhappiness is chiefly found in adolescent virgins;  
And youthful, timid adults who indulge in thoughts erotic;  
And the frigid, anæsthetic girls becoming so neurotic;  
And the apprehensive housewife frozen stiff by fear of more kids,  
Or whose husbands' flagging fervor calls for wreaths but not for orchids;  
And the grass and real widows with their hearts on sleeves a-waving,  
Overcome by foul frustration to a biologic craving;  
And the Romeos and Juliets, though senile, worn and flappy—  
Why, it doesn't seem as though there's anyone alive who's happy!  
(From J.A.M.A.)

## Service News and Notes.

Since the issue of the last number, two general meetings were held under the auspices of the Association on the 16th March 1938 and 19th March 1938. Dr. M. J. Santhanakrishna Pillay and Dr. (Miss) H. M. Lazarus described the experiences of their tours in Europe and America illustrating their talk with lantern slides and cinema.

A meeting of the *Executive Committee* was held on Saturday, 2nd July 1938. It was resolved to send a representation to the authorities on the unfairness of a cut in one's actual emoluments on promotion. Several members have thus suffered, as their special pay is not taken into account in giving them a personal allowance to cover the excess of their emoluments as assistant surgeons over their initial pay in the new higher scale.

*Retirements.*—During the period under review Dr. M. R. Guruswamy Mudaliar and Dr. V. R. Sundaresa Iyer have retired from service. We wish them long life and happiness in their retirement.

We are, however, glad of the honour conferred on Dr. M. R. Guruswamy Mudaliar by his appointment as Consulting Physician to the Madras General Hospital and that his services are still at the disposal of his colleagues

who wish to profit by his expert advice.

*Congratulations.*—We congratulate Rao Bahadur Dr. T. S. Tirumurthi on his appointment as Principal of the newly created Stanley Medical College, Madras. His pioneer work and the future of the College will depend mostly on what his initiative and persuasive powers with the authorities can procure for it. Our best wishes go with him in his very difficult task.

We learn with gladness and pride of the following academic distinctions achieved by our colleagues in the service:

F.R.C.S. (Edin.).—Dr. R. K. Tampan, Dr. R. Mahadevan, Dr. K. V. Ramanamurthy and Dr. K. Manjunath Rai.

D.M.R.E.—Dr. K. Manjunath Rai.

D.A. (R.C.P. & S.).—Dr. P. V. Francis.

M.P.H. (Johns Hopkins' Baltimore).—Dr. K. S. Viswanathan.

M.C.O.G.—Dr. P. V. Venkataswamy.

M.S. (Madras).—Dr. D. Subrahmanyam.

We understand that the Rockefeller Fellowship has been offered

this year to Dr. M. K. Krishna Menon of the King Institute, Guindy. In congratulating him we hope he will give as good an account of himself in America as his predecessors from our service had done.

We believe that Dr. K. V. Venkataraman, M.D., of the King Institute, Guindy, has been selected for appointment in the Indian Medical Research Department. Our loss is a gain to Research. We offer him also our heartfelt congratulations.

It is our pleasant duty to congratulate Dr. R. E. S. Muthayya, M.B.B.S., L.O., on his marriage which took place in May this year. He represents the second generation in one family in our service and because of that his

name is bound to be familiar to all our members.

Two new appointments at the Vizagapatam Medical College have just been made:—those, of Dr. T. Bhaskara Menon, M.D., D. Sc., M.R.C.P., as Professor of Pathology, and of Dr. N. Govinda Pandalai, M.D., M.R.C.P., as Professor of Bacteriology. We heartily congratulate them on their well deserved promotion.

*The Journal.*—Absolute indifference is the attitude of most members towards the Journal. A few have always done their best—all honour to them! The continuance of the Journal, as at present conducted, must be once for all decided at the next annual meeting.

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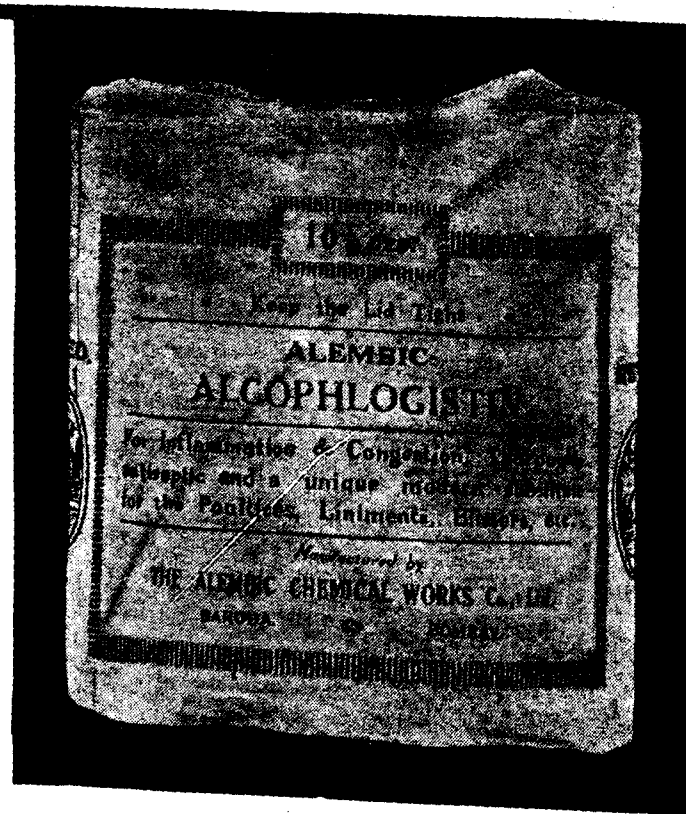
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## The Madras Medical Journal.

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## THE MADRAS MEDICAL JOURNAL

VOL. XVIII

OCTOBER, 1938,

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## CONTENTS.

|                                                                                  |         |
|----------------------------------------------------------------------------------|---------|
| 1. THE CHEMOTHERAPY OF BACTERIAL INFECTION                                       | PAGE    |
| —SULPHONAMIDE AND DERIVATIVES—A REVIEW                                           |         |
| By J. C. David, M.B., Ph.D.                                                      | ... 239 |
| 2. ORAL TREATMENT OF MALARIA WITH QUININE                                        |         |
| By G. Dinker Rau, M.D., D. Govinda Reddy, M.D., and<br>G. N. Rajagopal, M.B.B.S. | ... 250 |
| 3. NEOPLASMS OF THE KIDNEY                                                       |         |
| By N. Mangesh Rau, M.B.C.M., F.R.C.S.E.                                          | ... 254 |
| 4. CLINICAL MEMORANDA.                                                           |         |
| (a) TWO CASES OF EXTENDED BREECH IN A<br>PRIMIPARA                               |         |
| By R. G. Krishnan, F.R.C.S.                                                      | ... 264 |
| (b) TWO CASES OF SUSPECTED ECTOPIC PREGNANCY                                     |         |
| By R. G. Krishnan, F.R.C.S.                                                      | ... 265 |
| 5. GLEANINGS FROM CURRENT MEDICAL LITERATURE                                     | ... 268 |
| 6. NOTICE—DENTAL DIPLOMA.                                                        | ... 280 |
| 7. SERVICE NEWS AND NOTES.                                                       | ... 283 |

The  
**Madras Medical Journal.**

The Journal of the Madras Medical Association.

PUBLISHED QUARTERLY.

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**The Chemotherapy of Bacterial Infection.**

**SULPHONAMIDE AND DERIVATIVES—A REVIEW.**

BY J. C. DAVID, M.B., Ph.D.,

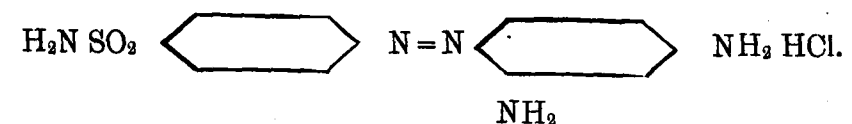
*Madras Medical College.*

In 1935 Domagk first published his results of the clinical trials of *Prontosil* in streptococcal infections. This is the hydrochloride of 4-sulphanimo 2: 4 diamino-azo-benzene, and is entirely non-toxic and has no physiological effect on circulation or unstriated muscle, etc. But, mice inoculated with 10 M.L.D. of *Streptococcus pyogenes* survived if from  $\frac{1}{10}$  to  $\frac{1}{50}$  of the maximum tolerated dose were given repeatedly either by mouth or by injection. This action has been confirmed in man. But *Prontosil* is entirely without action on bacteria *in vitro* and its mode of action was a complete mystery until the hypothesis, now gene-

rally accepted, was put forward that its action was due to conversion to sulphanilamide or *p*-amino benzene sulphonamide in the body. Sulphanilamide is found in urine when *prontosil* is given by mouth and a greater part of this substance is reduced in this manner in the presence of infection.

A number of such compounds are now in use and synonyms under which these are sold have led to much confusion.

**Prontosil** also called **Prontosil rubrum** or sulphamido-chrysoidin, is an azo-derivative containing two benzene rings and is meant for oral administration only:

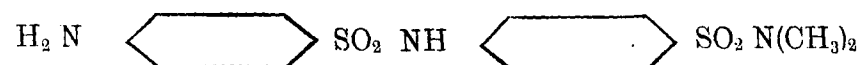


**Soluble Prontosil** is a still more complex compound and has three benzene rings. It is given by intramuscular injections.

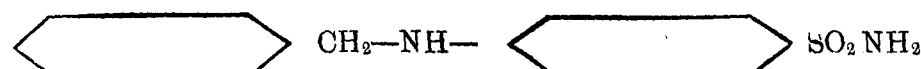
**Sulphanilamide** or *p*-amino benzene sulphonamide has the following formula :



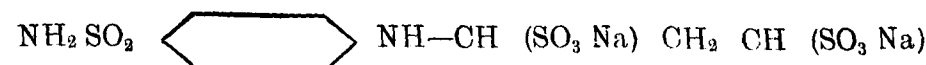
**Uleron** or *Diseptal* has the following chemical construction :



**Proseptasine** is



**Soluseptasine** is



*M. & B. 693* is 2 (*p*-amino benzene sulphonamide)-pyridine, also called 2-sulphanilyl amino pyridine and is still in the experimental stage.

**Absorption and Excretion of Sulphanilamide.**—Sulphanilamide is rapidly absorbed from the gut, the process being completed in four hours. It enters the blood at the same rate if given subcutaneously. Reaching a peak in about three hours, the concentration falls in a straight line to almost zero in 24 hours; thus a

This is also called *Streptocide* or *Prontosil album*, *Prontylin* *Cotsulanyde*, etc., and may be given by mouth, subcutaneously and intrathecally (0.8 per cent aqueous solution represents limit of solubility).

fully adequate concentration for therapeutic action persists after any single dose for about six hours. Four or six-hourly administration will therefore maintain this. Other theoretically effective substances like acridine dyes are excreted too rapidly. This persistence in the blood is due to the reabsorption (Marshall *et al*) in the renal tubules of 70 to 80 per cent of the drug in the glomerular filtrate. The rate of clearance increases with the rate of urine flow; and so the drug can, at will, be washed

out of the system by forced fluids and consequent diuresis; hence the importance of restricting intake of fluids. Sulphanilamide is not concentrated in any particular organ. It has been demonstrated in pleural and peritoneal effusions and in the spinal fluid. If the drug is given in divided doses over a period of time, equilibrium between absorption and excretion takes about three days to be established, and about the same time elapses after cessation of treatment before elimination is completed. Practically all the drug given can be recovered from the urine, excretion being delayed when the kidneys happen to be previously damaged. *Prontosil* is excreted in urine partly unchanged and partly as sulphanilamide, some of which is conjugated to form *p*-acetyl-amino-benzene sulphonamide.

Sulphanilamide has been found in the cervical secretion and menstrual fluid but in amounts too small for any bactericidal action. It is also excreted in breast milk, both free and as the acyl derivative. It is transmitted to the placenta and foetus. Until more is known of the tolerance of human foetus and of the new born for sulphanilamide, the drug should be administered only with the utmost caution during pregnancy and lactation (Adair *et al* 1938).

**Anti-bacterial Action.**—It is perhaps necessary to point out that the use of these drugs imperatively demands a bacteriological as well as a clinical

diagnosis. These are *specifics* not for septicæmia, meningitis, or pneumonia, but for infections by certain bacteria wherever situated and have little or no effect on other species.

*Prontosil* has no action on bacteria *in vitro*, but its reduction product sulphanilamide was found to delay the growth of a small inoculum of *streptococcus hæmolyticus* (30 to 50 cocci) at a dilution of 1 in 10,000 for two or three days. But even at a strength of 1 per cent it was not able to affect the growth of a huge inoculation of 300,000,000 organisms, but it was able to slow down the rate of multiplication of an inoculum to  $\frac{1}{10}$  that number. Also, sulphanilamide in a dilution of from 1 in 13,000 to 1 in 18,000 in human blood could completely, or almost completely, destroy an inoculum of 3,500 cocci per 5 c.mm. On the other hand, *prontosil* had no action under similar conditions.

Animals were given sulphanilamide and *prontosil* by mouth. It was then found that small inocula of streptococci were destroyed by the blood under these conditions. Similarly in normal persons and those infected with streptococci, the administration of large doses of *prontosil*, *prontosil S.* or sulphanilamide increased the bactericidal power of the blood.

From the observation that neither *prontosil* nor *prontosil S.* when added to blood can check the growth of organisms while internal administration of either drug to man or animal confers

that power on it, it is deduced that both can give rise to sulphanilamide in the body, as has been shown by direct experiment; and that sulphanilamide has a direct damaging action on streptococci; either actually killing them or at least preventing their growth; the limited numbers upon which the drug acts *in vitro* correspond to those found in the blood stream and elsewhere in widespread infection.

Fleming (1938) found that the anti-bacterial power of *M. & B. 693* resides in the serum and that the efficacy of leucocytes was not increased. The patient's serum not only inhibits the growth but also inhibits the production by *S. pyogenes* and pneumococcus of substances which alter the blood. When added to human blood or contained in the blood of patients taking the chemical it does not prevent encapsulation of pneumococci but a more likely of action is simple inhibition of growth (and possibly of toxin production) and that the decapsulation occurs as the result of some other autolytic process.

Fritz Meyer (1938) believes that sulphanilamide acts only in organisms which possess a certain amount of natural resistance. He observes that cases of severe streptococcal infection, as for instance, puerperal fever, which do not respond to sulphanilamide may be cured by additional treatment with anti-streptococcal serum. Inasmuch as the chemotherapeutic agent can only exert its action under co-operation of the natural defence system of

the infected organism, this resistance must be supported by all possible means (*immune* transfusions, vitamins, etc.). The toxic by-effects of the drug can be avoided by combining serum and sulphanilamide as this combination makes the reduction of the sulphanilamide dosage below the point of danger possible. Fleming (1938) is also of opinion that the actual destruction of the organisms is effected by the natural defences of the body, although these may be unable to function successfully unless the growth of the bacteria has been restrained by the chemical. A patient infected with a very sensitive hæmolytic streptococcus is likely to be saved even when the natural immunity is low. If, however, this patient is infected with a less sensitive microbe, such as a particular type of pneumococcus, then the serum of such a patient is almost impotent in the presence of his own leucocytes, although when healthy leucocytes are present, growth is completely restrained. In the case of an infection with this microbe, therefore, it is unlikely that a drug like *M. & B. 693* would be effective unless the natural defensive mechanism of the body was in good condition.

Some authorities are not yet completely convinced that the action is solely due to the liberation of sulphanilamide *in vivo*. One objection is that weight for weight prontosil is therapeutically the more effective; the amount of sulphanilamide which it liberates is distinctly less than the amount of sulphanilamide

itself which has to be given to achieve the same results. Another point is that other therapeutically active compounds such as *uleron*, are not reduced to sulphanilamide in the body. Thirdly, while prontosil was found to be efficacious in curing mice infected with the *virus* of choroid meningitis, sulphanilamide had no such effect.

With regard to the *relation of chemical structure and anti-bacterial action*, it was found that removal of the amino group from the *p*- to the *o*- or *m*-position destroyed the activity. Again, a similar result was found to follow any attempt to substitute another radical for either the amino or the sulphamido group. From these results, it seems clear that there must be: (1) an amino-group attached to the benzene ring; (2) a sulphamido group similarly attached; and (3) that these groups must be in the *p*-position, one to the other.

### Therapeutic Action.

(1) IN STREPTOCOCCAL INFECTIONS.—It is important to recognise that susceptible infections are only those due to *Streptococcus pyogenes*; those due to *S. viridans*, such as subacute bacterial endocarditis, and to *S. faecalis* (urinary infection due to this organism) are uninfluenced.

In *Erysipelas* uniformly good effects are secured. Prontosil was found to arrest the spread forthwith. Fever abates within 24 hours. Snodgrass, Anderson and Rennie (1938) are of the opinion that the choice of the drug to be

employed can be left to individual preference. The method of administration to an adult patient is recommended to be: (i) Sulphamido chrysoidin (Prontosil) 1.5 g. every 4 hours, *i.e.*, 9 g. per day, until cure is established; thereafter 1 g. *t.d.s.* for a further period of 14 days; (ii) Sulphanilamide 1 g. every 4 hours, *i.e.*, 6 g. a day until cure is established; thereafter 1 g. 3 times a day for a further period of 14 days. All other drugs must be avoided during the period of specific treatment a list of suitable purgatives should be given to the patient, the use of enemata explained and explicit instructions given regarding diet.

In *Tonsillitis and Scarlet Fever* favourable reports have been made, the streptococcus disappearing from the throat very quickly.

In *Puerperal Fever* the mortality has been very greatly reduced. The effect of prontosil in severe cases is said to be superior slightly to that of sulphanilamide.

(2) IN PNEUMOCOCCAL INFECTIONS.—*In vitro* and *in vivo* experiments on animals have shown that pneumococcus is also susceptible to sulphanilamide. It seems clear also that type III infections are more amenable to the treatment than others, a singular fact all the more fortunate since this type is entirely uninfluenced by serum. Encouraging results have been obtained by the use of *M. and B. 693* (May and Baker) a pyridine derivative of sulphanilamide. Serum should not be withheld.

Dyke (1938) reports a case of pneumococcal septicæmia successfully treated with M. & B. 693. The septicæmia was subdued after the first 9 g. Reid and Dyke (1938) report recovery in a case of pneumococcal meningitis in a girl of 7. Within 12 hours of starting treatment the pulse, respiration and temperature fell rapidly. But progress was slow. A total dosage of 45 tablets or 22.5 g. in 10 days was required to cure this case.

(3) IN STAPHYLOCOCCAL INFECTION, clinical verification is lacking although experimentally it is known that *S. aureus* is at least moderately susceptible to this treatment. Uleron (Hanschell 1938) in doses of 3 g. in 24 hours for 5 days was found very effective and non-toxic.

(4) IN MENINGOCOCCAL INFECTION there is clear evidence of therapeutic efficacy, but perhaps not yet enough to decide the optimum method of administration or the indication for serum treatment in addition. Some observers think that combined treatment with the drug and serum gives better results. The combined treatment of serum and prontosil derivatives were found very efficacious in the recent epidemic of cerebrospinal meningitis in Madras.

(5) IN GONOCOCCAL INFECTION.—Reports vary. While almost all authors report good results, a minority of patients entirely fail to respond. O'Hanlan's statement that the average

period of invalidity among troops at Aldershot has been reduced from 62 to 21 days carries conviction. Treatment should be begun in the acute stage. Complications, both local and metastatic respond well and the rapid disappearance of gonococci from exudates in distant situations as well as the urogenital tract is a usual finding. Massive doses of sulphanilamide are recommended by some workers. Prontosil is less effective. Uleron is said to be superior and while continental workers are in favour of this, English clinicians prefer M. & B. 693, which they consider to be more constant in producing rapid and lasting cures. It is suggested that treatment with uleron and similar compounds should be begun after the first week so as to mobilise bodily defence. Hanschell (1938) found uleron more effective in gonorrhœa in the male than any other similar preparation. Uleron is effective in early gonococcal infection 5 to 14 days old but even more effective in infections of 21 days and over. Some workers have reported complications like peripheral neuritis, palsy, hepatic and renal damage after uleron.

Bowie (1938) records markedly quick cures in gonococcal urethritis and ophthalmia neonatorum with M. & B. 693. The results were better than with uleron and complications were less. Michie and Webster (1938) treated gonorrhœal ophthalmia in children with success with 0.25 g. of M. & B. 693 twice a day. Fernandez (1938) had similar success in adult cases.

McElligott and Cokkinis (1938) believe that uleron is not superior to sulphanilamide in the treatment of gonorrhœa and has a greater incidence of toxicity. Their experience of 491 male cases and 142 female cases analysed in their report shows that the best results with sulphanilamide treatment in gonorrhœa can be obtained only by a specialised technique of administration and that incorrect or haphazard therapy is followed by a large number of failures. *A degree of immunity seems to be essential to the attainment of optimum results, hence the importance of timing the chemotherapy correctly and combining it with immune therapy.*

With the optimum technique advised, 80 per cent of male patients are cured with one course of three weeks, treatment, although the clinical manifestations usually clear up within the first week. With additional courses in cases of resistant or relapsed cases over 90 per cent success can be obtained. In men vaccine treatment is started at once within the first week of symptoms and continued twice weekly (starting with 5 and increasing to 100 million) throughout the chemotherapy. The irrigations, etc., are maintained. Sulphanilamide is started 8 to 10 days after appearance of discharge and continued for full three weeks. The daily dosage, which varies with weight, is usually 4 g., two 0.5 g. tablets being taken with a glass of water after the four daily meals. After two weeks this may be diminished to 3 g. Apparent cure is expected in 2 to 7 days. After 3 weeks the treatment is

suspended and the patient attends weekly for prostatic bead tests, 3 to 4 weeks later, prostatic massage, vaccine (400 to 500 mill.) or alcohol provides the provocative test. After passing all tests the patient is kept under observation for a further period of 6 to 8 weeks.

In acute cases attending after the first week, the chemotherapy is started at once. In chronic cases the dosage need not exceed 3 g. daily and the total period may be cut down to about 17 days, while a mixed gonococcal vaccine may be given with advantage.

In women, the treatment is similar. Owing to their lighter average weight, 3 g. is an adequate daily dose. At the end of 3 weeks if all tests are negative, treatment is stopped and the patient is examined fortnightly for one month and then after each period for a further two months, when if after a provocative vaccine injection, tests are negative the patient is regarded as cured. In chronic cases stovarsol pessaries are an additional recommendation. The conditions in women are not as satisfactory as in men, as the former are more susceptible to the minor toxic effects of sulphanilamide. *Interruption of the chemotherapy in the earlier weeks must be prevented at all costs.*

(6) IN URINARY INFECTIONS.—Kenny *et al* treated 46 cases of *B. Coli* infection 16 of which were of pyelitis of pregnancy, and invariably secured a

sterile urine within a week, often within 3 days. They found sulphanilamide superior to and cheaper and pleasanter than mandelic acid. It has been shown that sulphanilamide is much more bactericidal in an alkaline than an acid urine and the drug itself causes the secretion of an alkaline urine, probably by interfering with tubular reabsorption of bicarbonate and bases. In the urinary tract at least sulphanilamide seems to be directly bactericidal and urine containing it destroys added bacteria.

This treatment and mandelic acid complement one another, and have separate indications. Mandelic acid requires a highly acid urine and good renal function; sulphanilamide acts best in the presence of renal damage. Mandelic acid is effective against *S. faecalis* infection, but sulphanilamide fails; mandelic acid is usually powerless against *Proteus* infection, but sulphanilamide succeeds. Sulphanilamide can be given in the acute stage. But mandelic acid is less harmful being less toxic. With sulphanilamide there is absence of nausea and digestive disturbances. The doses usually given are 0.5 or 0.6 g. *t.d.s.* for 5 to 7 days orally.

(7) TREATMENT OF CHANCROID WITH SULPHANILAMIDE.—B. A. Kornblith, A. Jacoby and M. Wishengrad observed the effect of this drug on a series of 45 cases of chancroid. The lesions which were positive for Ducrey's bacillus ranged from 18 mm. ulcerations on the prepuce to complete slough-

ing of the glans penis. The average duration was from four weeks to two years prior to treatment. Preliminary treatment with soap and water for a period of one week was instituted and if no results were obtained sulphanilamide was then given, consisting of the administration of 80 grs. of the drug in divided doses for the first five days and 40 grs. in divided doses for nine additional days. The treated cases healed promptly at the end of two weeks. No recurrence has occurred after six months. No ill effects were noticed. The treatment was ambulatory.

(8) IN GAS GANGRENE the results published are encouraging, sulphanilamide succeeding even where gangrene set in after prophylactic antitoxin.

(9) (i) IN BRUCELLA MELLITENSIS INFECTION.—According to Neumann (1938) and others prontosil and other sulphanilamide preparations so far represent the most convenient treatment for undulant fever and may find a valuable place in the fight against this creeping and long drawn out disease.

(ii) IN BRUCELLA ABORTUS INFECTION.—Dalrymple—Champneys (1938) reports on 35 cases treated with prontosil, prontosil soluble and sulphanilamide compounds. The results although not completely successful in all cases, justify the continued trial of these drugs in the treatment of these infections.

(10) Further reports are needed before we can assess its value in typhoid fever, etc.

11. The prophylactic value of these compounds in various infections is doubtful.

12. LOCAL APPLICATION.—Purdie and Fry (1937) describe a case of chronic wound infection due to hæmolytic streptococcus, following puerperal sepsis also streptococcal three years previously, where, after various operative procedures and actinotherapy had failed to give relief, oral administration of sulphanilamide in doses of 1 g. *t.d.s.* (total 94 g.) with local treatment with the same drug (1 per cent solution and dusting) was followed by sterilisation of the wounds within three weeks and complete healing in six weeks.

13. IN EXPERIMENTAL PERTUSSIS in mice, Cruikshank (1938) found that the survival rate after infection was higher in those treated with M. & B. 693.

**Dosage and Mode of Administration.**—Particulars have already been given under specific heads. Oral administration usually serves all purposes, except perhaps the immediate treatment of meningitis, when intrathecal injection of a 0.8 per cent solution in saline may be desirable. The solution may also be given subcutaneously, if necessary in large volumes (700 c.c. has so been given as an initial dose) when swallowing or alimentary absorption is at fault. An alternative in these circumstances is to inject Prontosil soluble intramuscularly (intravenously it is badly tolerated and intrathecal is dangerous).

Most authors agree that a large initial dose is desirable (3 to 5 g. or more of sulphanilamide) in order to attain an adequate blood level as soon as possible. Long and Bliss suggest as a rule for total daily dosage 1 g. of sulphanilamide per 20 lb. body weight (maximum 5 g.) and 1 c.c. prontosil soluble (2.5 per cent solution) per 1 lb. (maximum 120 c.c.). Daily doses of about 5 g. can produce a maximum blood concentration of 5 to 7 mg. per 100 c.cm. and this is considered satisfactory in mild and moderate infections. These doses have often been exceeded. Massive doses have been tried in the treatment of gonorrhoea extended over 3 weeks, as for example, in the Venereal clinic in the Madras General Hospital. Children require proportionately larger doses. In less severe infections such large doses may not be necessary but it is safer to err on the side of giving too much rather than too little, as the toxic symptoms caused by 4 g. doses are slight and not alarming. The drug should not be stopped too soon as recurrence of infection may follow.

**Toxicity.**—The toxic manifestations which appear in the course of treatment with sulphanilamide seem to occur on a basis of sensitivity and idiosyncrasy. The latter, while apparently rare, is serious and the former, while more common, is usually mild but may become serious if ignored (Bannick *et al* 1938). Most individuals seem to show some sensitivity when the initial doses of the drug are large or when

the total administered amount is considerable. The toxic manifestations which occur with such doses are usually mild and consist largely of malaise, anorexia, nausea, vertigo and tinnitus. These symptoms may be due to an acidosis caused by the excretion of bicarbonate and bases due to diminished reabsorption in the renal tubules. With continuous doses these symptoms may be followed by cyanosis, abdominal cramps, diarrhoea, cutaneous lesions, fever, paræsthesias, and other more serious complications.

*Cyanosis*, in which the patient exhibits a strikingly blue colour, may be due to various causes:

(a) *Methæmoglobinæmia* may occur, as with other benzene compounds but is not serious and may clear up rapidly, especially if oxygen is given. (b) *Sulphæmoglobinæmia* may occur when sulphates are given concurrently with certain drugs like pyridium and acetphenitidin. It is said that the formation of this compound from hæmoglobin and  $H_2S$  is catalysed by many substances especially amino compounds. But *in vitro* experiments have not succeeded in producing this result when sulphanilamide was used. But still, it has been suggested that the administration of magnesium sulphate just before or at the same time as the sulphonamides will cause the development of intracorpuscular sulphæmoglobin, (perhaps the  $H_2S$  is absorbed from the gut in greater quantities in the presence of much fluid in the lumen of the gut) and measures for averting it

### The Madras Medical Journal

are directed to preventing the absorption of  $H_2S$  from the bowel and include a low residue diet and the avoidance of all purgatives, except liquid paraffin. This condition may be very serious and even oxygen may be of little value. In some cases 6 weeks may elapse before all traces of sulphæmoglobin is got rid off.

*Agranulocytosis* has been recorded but fortunately is uncommon and perhaps is due to individual idiosyncrasy.

*Acute anæmia* has been so far recorded in three cases.

*Central nervous symptoms*, such as drowsiness may follow doses of 1 g. or more. Massive doses produce a feeling of extreme weakness and mental apathy. Optic neuritis has been reported in one case.

*Drug fever* is said to have occurred after a latent period of about a week. It may also be due to a reaction due to products of lysed bacteria.

*Jaundice* has been noted in two cases in which death occurred and in which possibly hepatic damage had pre-existed. Sulphanilamide may therefore aggravate an already existing hepatic damage. Mild attacks of jaundice usually subside rapidly when use of the drug is discontinued and intake of fluids is forced. These two measures are of extreme importance in combating toxæmia due to the sulphonamide group

### The Chemotherapy of Bacterial Infection

and may be reinforced by the use of transfusions of blood or oral administration of bone marrow when disturbances in the blood occur.

The blood offers an index of toxicity even more important than the symptoms and a decrease in the hæmoglobin content or in the R. B. C. count or leucocyte count must be taken as evidence of a dangerous complication which necessitates immediate discontinuance of this form of therapy.

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#### A PRESCRIPTION

Gentlemen: I offer you a pet prescription. One that perhaps has escaped the attention of even the Journal's renowned Fantus. It has a limited field of application, unfortunately. You see it's a tonic for a "run-down" son of Aesculapius. Here it is:—

R  
Enthusiasm gr i  
Understanding gr i  
Skill 3i  
Thoroughness 3i  
\* Comp. Tr. Faith qs ad 3iv

Sig. A soulful P.R.N.

\* Old-timers are familiar with this. It may be unknown to a few of the younger sons of Aesculapius, however. The compound is faith in God, oneself, and one's fellow man.

(J.A.M.A.)

## Oral Treatment of Malaria with Quinine.

BY G. DINKER RAU, M.D., D. GOVINDA REDDY, M.D..

AND G. N. RAJAGOPAL, M.B.B.S.

*Madras General Hospital.*

Quinine for the treatment of malaria has been known to the West for over three centuries but in spite of the enormous amount of research since then its exact mode of action still remains a mystery. It cannot be that it acts directly on the parasite and kills it, for concentrations as high as 1 in 10,000 have failed to kill the parasite *in vitro*, while the concentration of quinine in blood in therapeutic doses of 30 grs. a day does not exceed 1 in 100,000 at any time. It is therefore presumed that its action on the parasite is an indirect one.

Recent research shows that quinine when given in therapeutic doses stimulates the activity of the cells that constitute the reticulo-endothelial system, and it has further been shown that immunity in malaria does not in any way differ from immunity in other diseases and is a function of the reticulo-endothelial system. Quinine therefore probably acts by stimulating the production of immune bodies and making conditions unsuitable for the growth and multiplication of the parasite in the human body.

This naturally raises the question: "What is the optimum

dose of oral quinine in the treatment of malaria?" There are two methods of administration.

(1) Full doses of quinine, about 30 grs. a day, are administered under the belief that the body should be sterilized of the infection as quickly as possible and prevent the parasites from becoming resistant to quinine.

(2) The other method is to administer small doses, about 5 grs. a day, for a longer period and thus avoid the toxic effects of quinine. It does not believe that these small doses produce a quinine resistant parasite except for the gametocytes of malignant tertian malaria which are little affected by quinine.

The effect of giving big doses is well known to most of us. Quinine is a strong irritant of the alimentary tract and is a severe poison to the tissues. It produces gastritis, enteritis, loss of appetite, ringing in the ears, deafness which is sometimes permanent, dimness or loss of vision, mental depression and cardiac weakness. In some cases it also produces albuminuria. Apart from these well-known effects we are of opinion that these doses definitely depress the reticulo-endothe-

lial system and actually delay the development of immunity. We also believe that they tend to raise the relapse rate.

On the other hand the giving of small doses of quinine, about 5 to 10 grs. a day, while avoiding these serious toxic effects controls the symptoms of malaria as efficiently as the bigger doses and we believe definitely tends to lower the relapse rate. One of us (G. D. R.) who has been trying the effect of these small doses for the past 3 or 4 years has had very encouraging results, and among the police of Vizagapatam District, who could be kept under fairly strict control, the relapse rate has at least been no higher than that under the bigger doses. We regret we cannot be more definite than this considering how difficult it is to follow up cases in India or to prevent re-infection of a case.

Appended are the results of

small doses of quinine on 21 patients treated in the medical wards of the General Hospital under our care during the past three months. The routine that has been followed in the treatment is as follows:—

The patient is given an initial saline purgative and is put on a mixture containing 5 grs. of quinine hydrochloride, 30 grs. of citric acid and water 3 ozs. One ounce of the mixture is given three times a day, an hour after food. The advantage in giving the mixture an hour after food is that it prevents irritation of the stomach and intestines when given on a full stomach and also helps its absorption. Blood smears of each patient are taken every day and searched carefully for parasites and the results noted. The quinine is continued for a total period of 15 days from the commencement of treatment.

| Name.                      | Age. | Sex.   | Date of Admis-<br>sion. | Date of Dis-<br>charge. | Variety and Stages of<br>Parasites found<br>and when.                                                          | Date of Dis-<br>appearance<br>of Parasite<br>from Peri-<br>pheral blood. | Quantity of<br>Quinine sulph<br>given when<br>temp. touched<br>normal. | Remarks.                               |
|----------------------------|------|--------|-------------------------|-------------------------|----------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|------------------------------------------------------------------------|----------------------------------------|
| 1 Arumugam                 | 67   | Male   | 18-8-1938               | 24-8-1938               | Benign Tertian Rings<br>on 19-8-1938                                                                           | 21-8-1938                                                                | 20 grs.                                                                |                                        |
| 2 Babu Jan                 | 22   | Male   | 4-8-1938                | 9-8-1938                | B.T. Rings and Schizonts<br>on 6-8-1938                                                                        | 8-8-1938                                                                 | 15 grs.                                                                |                                        |
| 3 Bakiamma                 | 30   | Female | 26-9-1938               | 6-10-1938               | B.T. Rings on 27-9-1938                                                                                        | 28-9-1938                                                                | 15 grs.                                                                |                                        |
| 4 Chellappan               | 30   | Male   | 5-9-1938                | 11-9-1938               | B.T. Rings on 5-9-1938                                                                                         | 8-9-1938                                                                 | 12 grs.                                                                |                                        |
| 5 Deva Doss                | 20   | Male   | 25-8-1938               | 31-8-1938               | B.T. Rings found on<br>28-8-1938                                                                               | 29-8-1938                                                                | 10 grs.                                                                |                                        |
| 6 Ellappan                 | 25   | Male   | 6-10-1938               | 12-10-1938              | Malignant Tertian Rings<br>and crescents on 7-10-1938                                                          | 9-10-1938                                                                | 10 grs.                                                                | Crescents persisted<br>till discharge. |
| 7 Gangan                   | 11   | Male   | 5-9-1938                | 10-9-1938               | Benign Tertian Rings and<br>Schizonts on 5-9-1938                                                              | 8-9-1938                                                                 | 12 grs.                                                                |                                        |
| 8 Govindan Nair            | 26   | Male   | 8-9-1938                | 12-9-1938               | B.T. Rings and Schizonts.<br>Heavy infection on<br>8-9-1938                                                    | 11-9-1938                                                                | 12 grs.                                                                |                                        |
| 9 Govindasami              | 18   | Male   | 26-9-1938               | 3-10-1938               | Malignant tertian rings and<br>crescents. Murrers ovals<br>in every corpuscles with<br>a parasite on 26-9-1938 | 28-9-1938                                                                | 20 grs.                                                                | Crescents persisted.                   |
| 10 Hari Krishna<br>Naicker | 28   | Male   | 4-7-1938                | 8-7-1938                | Benign Tertian parasite<br>from Ring to Schizont<br>5-7-1938                                                   | 8-7-1938                                                                 | 12 grs.                                                                |                                        |

|                    |    |        |            |            |                                                                          |            |         |                                         |
|--------------------|----|--------|------------|------------|--------------------------------------------------------------------------|------------|---------|-----------------------------------------|
| 11 Krishnan        | 18 | Male   | 3-10-1938  | 12-10-1938 | Malignant Tertian Rings<br>Heavy infection on<br>4-10-1938               | 8-10-1938  | 15 grs. |                                         |
| 12 Manjunathan     | 21 | Male   | 14-7-1938  | 19-7-1938  | Benign Tertian parasite all<br>stages, Ring to Schizont.<br>on 15-7-1938 | 18-7-1938  | 15 grs. |                                         |
| 13 Moses           | 25 | Male   | 12-7-1938  | 18-7-1938  | B.T. Parasite all stages,<br>Rings to Schizont, on<br>13-7-1938          | 16-7-1938  | 15 grs. |                                         |
| 14 Mohideen        | 36 | Male   | 4-7-1938   | 7-7-1938   | B.T. Full grown Schizont<br>on 4-7-1938                                  | ...        | ...     | Patient was dis-<br>charged at request. |
| 15 Manavala Pillai | 25 | Male   | 30-6-1938  | 4-7-1938   | B.T. Rings and Schizonts<br>on 30-6-1938                                 | 3-7-1938   | 15 grs. |                                         |
| 16 Raja Ram        | 18 | Male   | 27-6-1938  | 3-7-1938   | B.T. Rings on 27-6-1938                                                  | 29-8-1938  | 25 grs. |                                         |
| 17 Seshachalam     | 23 | Male   | 1-9-1938   | 7-9-1938   | B.T. Rings and Half grown<br>on 2-9-1938                                 | 5-9-1938   | 18 grs. |                                         |
| 18 Somanna         | 30 | Male   | 15-8-1938  | 22-8-1938  | B.T. Parasite, all stages<br>found 17-8-1938                             | 19-8-1938  | 18 grs. |                                         |
| 19 Venugopal       | 26 | Male   | 19-9-1938  | 24-9-1938  | B.T. Rings on 19-9-1938                                                  | 22-9-1938  | 15 grs. |                                         |
| 20 Vedambal        | 33 | Female | 22-8-1938  | 29-8-1938  | B.T. Rings on 23-8-1931                                                  | 25-8-1938  | 18 grs. |                                         |
| 21 Kesavan         | 30 | Male   | 13-10-1938 | 16-10-38   | B.T. Full grown in plenty<br>on 13-10-1938                               | 16-10-1938 | 15 grs. |                                         |

## Neoplasms of the Kidney.

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These are found in greater variety in the kidney than elsewhere in the body. But benign growths are few and rare while malignant ones are more common. In this it resembles the genital gland, testis.

Benign neoplasms form less than 7 per cent of renal growths. They are more interesting from pathological than surgical point of view as they rarely give rise to any symptoms.

1. *Adenomas*.—These occur as small tumours in the sub-capsular and less often in the medullary areas and may reach the size of a cherry. They are usually single, rounded, greyish-white or pink in colour and surrounded by a definite capsule. They give rise to no symptoms and are usually discovered *post-mortem*. They consist of a mass of tubules packed together, but glomeruli are absent. Ducts may show dilatations with papillary ingrowths lined with cylindrical epithelium, or a tubular or alveolar arrangement consisting of hollow or solid masses of cylindrical epithelium.

So far a transitional stage between these and malignant nephromas has not been reported. But such a change is likely.

These tumours may remain symptomless throughout life.

Hæmaturia and pain may set in suddenly after the onset of a malignant change.

2. *Lipomata*.—Are usually small and multiple and situated under the capsule. Occasionally a large one may be met with.

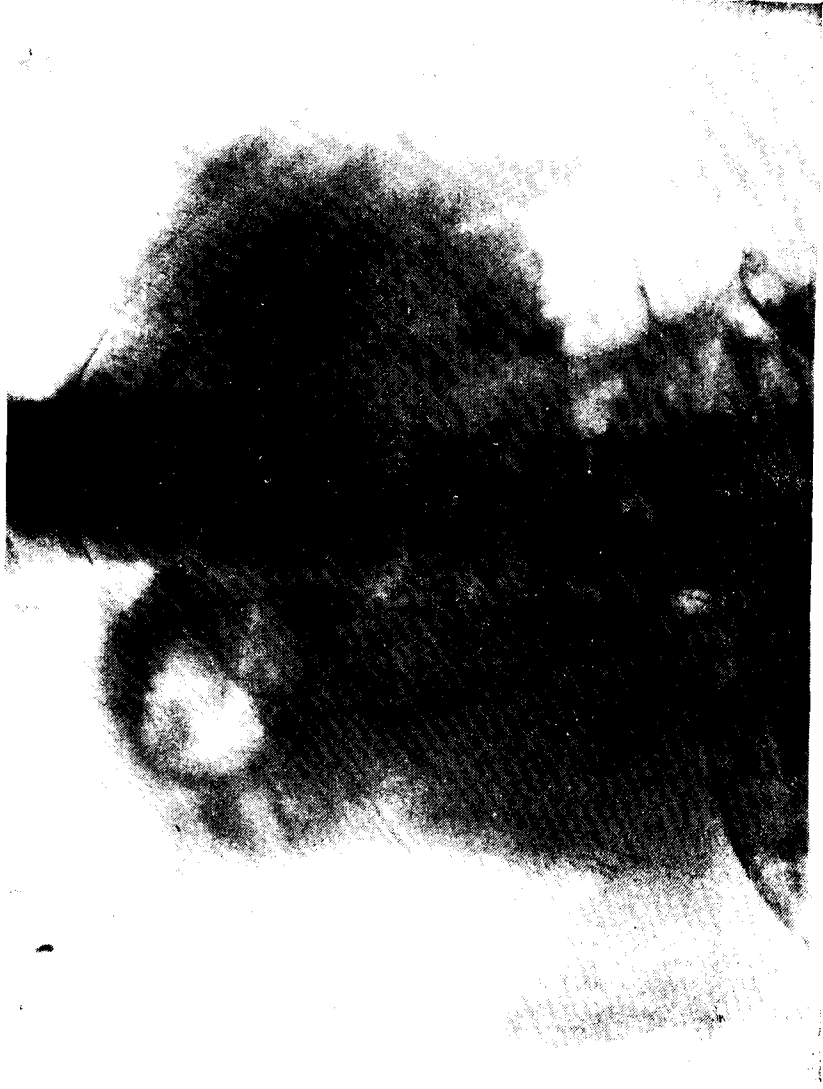
3. *Fibromas*.—Pure fibromas are extremely rare and may be met with as small fibrous nodules in the cortex or medulla. They are often congenital.

4. *Leiomyomas*.—Are very rare and occur as small nodules of smooth muscle fibres under the capsule. These and the fibromas are probably embryonal rests liable to show sarcomatous change. Diagnosis of these innocent tumours is rarely possible. The small ones are made out only *post-mortem*. The larger ones are indistinguishable from malignant growths.

5. *Hæmangiomata*.—Are also rare and do not grow to a large size. They may be either of the capillary or cavernous type. They may occur on the outer surface of the kidney when they give rise to no symptoms. But they are more common on the mucous surface of the renal pelvis or calyces giving rise to painless hæmaturia. In some cases they are of the nature of varix giving similar symptoms.



1. Ascending pyelogram. Note the deformity of left renal pelvis and tumour in the lower pole of kidney. Note the secondary deposits in the lungs.



II. Excretion pyelogram. Note the large tumour, demarcated by a calcified guinea worm, at the lower pole of kidney. The left renal pelvis is not visualised.



III. Radiogram of left kidney after nephrectomy. Note the deformities of the calyces especially the lower. Note the calcified guinea worm.

**Malignant Neoplasms.**

These can be divided into two groups:—(a) those arising from the kidney, (b) those arising from the pelvis and ureter.

Renal malignant tumours may be divided into two main groups:—(a) Renal embryomas which are congenital tumours of infancy and childhood, (b) Malignant nephromas of adult life.

*Renal Embryomas.*—These are malignant tumours arising from the undifferentiated cells of the myotomes of the renal region in the embryo. These cells may be either displaced or arrested in their natural growth and may later grow into tumours. These cells are totipotent and hence the tumours may contain every kind of tissue. They have been called teratoid tumours, Wilm's tumours, adeno-myo-sarcomas, etc.

They occur usually in infancy or before the third year and very rare after 18 years. The incidence is equal in both sexes. They have been seen in the foetus and new born child. These tumours have a resemblance to the retro-peritoneal sarcomata of embryonal type that may occur in the retro-peri-renal area. The hilum of the kidney is the favourite site, the kidney being spread out on its surface as a rim of compressed tissue. The growth seldom invades the parenchyma. They form large rounded tumours of firm consistence, yellowish-white in section with areas of hæmorrhagic and mucoid degeneration. Microscopic examination shows the tumour to be composed of small

round or oval cells of sarcomatous nature lying in a loose oedematous connective tissue. Tubules lined with columnar epithelium may be found embedded in the less differentiated cells and sometimes islands of cartilage and muscle fibres may also be present. The cells do not show an orderly arrangement. They consist of large amounts of embryonic connective tissue with a small amount of epithelial element in the form of acini or tubules lined by cuboidal or columnar epithelium. Very rarely a true teratoma or a dermoid may be present. The surface is usually smooth and not adherent to surrounding viscera. The malignant change may be either sarcomatous or carcinomatous and metastasis is by blood stream.

*Signs and Symptoms.*—This tumour is most commonly seen in children in the early years of life. Palpable tumours are present long before any other signs are noticed. An increasing abdominal distension, malaise, loss of weight, emaciation, pain, enlargement of abdominal veins, ascites, oedema of legs, constipation and other pressure symptoms are the usual ones for which the child is brought. Urinary symptoms are absent. Hæmaturia is rare occurring in 10 per cent. Prognosis is very poor; death occurs in about three to five years.

*Treatment.*—If a large tumour is felt, deep X-ray therapy should be tried first. Embryonic tissue is very sensitive to radiation therapy. When reduced in size a nephrectomy should be done to

be followed by another course of deep X-ray therapy. Prognosis, however, is not satisfactory and life is only prolonged by this treatment.

**Renal Sarcomas.**—These form only a small proportion of renal malignant growths. These may consist of round, spindle or mixed cells and often include striped or unstriped muscle fibres. They are really embryomas and may even show inclusions of Wolffian body or embryonic rests from metanephros.

#### Malignant Nephromas.

These are tumours of adult life but their classification is unsatisfactory and differences of opinion prevail among pathologists. They are all carcinomas, and three types are recognised: (a) Hypernephroma, (b) Adenocarcinoma, (c) Alveolar adenocarcinoma.

**Hypernephroma.**—This name was given by Grawitz and Lubarsch as they believed that the tumour arose from supra-renal rests in the kidney owing to a resemblance of its cells to those of zona fasciculata of adrenal gland. But neither intensification of sex characters occurs nor is adrenaline found in the tumours. Albarran and Imbert speak of these tumours as clear-cell ephitheliomas. Some consider them as papillary adenocarcinoma of renal origin. Again others consider them as arising from rests of Wolffian tubules. Over 60 per cent of malignant growths of kidney belong to this group. They are most common in the fourth and fifth decades

of life and may effect any part of the kidney.

**Pathology.**—In most, the cell cytoplasm is greatly distended with droplets of lipoid material and show small round dark-staining nuclei. In ordinary preparations the fat droplets are dissolved away leaving the cytoplasm as a translucent fine network and hence were named "clear cell epitheliomas" by Albarran. The fat droplets can, however, be stained by fat stains in frozen sections and are seen to be doubly refractile under the polarising microscope. The cells may be arranged in solid columns, acini or abveoli, the groups of cells being separated by delicate capillaries and a small amount of connective tissue. When the cells are arranged in strands separated by the vascular connective tissue it resembles that of adrenal cortex. But a careful examination always reveals a tubular arrangement. When tubular arrangement is more general they are usually described as adenocarcinomas. In some the lumen may be distended into cysts with intracystic papillary projections or show a papillomatous arrangement round a vascularised connective tissue core and thereby resemble a papillary adenocarcinoma. In others again there may be an alveolar arrangement of cells resembling an alveolar adenocarcinoma.

The tumour is very liable to cystic degeneration and necrosis which may be extensive or only affect the cells at the centre of an acinus. In the later stages

either multiple small cysts or a few large blood cysts may form to such an extent as to reduce the tumour tissue to a mere network and the lining layer of the spaces to a single layer of cells. The tumour may be made of cyst-like cavities separated by thin trabeculae, and lined by a single layer of cuboidal or flat epithelium. From the trabeculae an enormous number of thin branching papillae covered by similar epithelium may spring and completely fill the cavity resembling a papillary cyst-adenoma, but these cysts do not communicate with the renal pelvis. With this there may be invasion of kidney substance with strands and cords of closely packed and apparently carcinomatous cells without the distended cytoplasm and with no resemblance to hypernephroma cells. These may be only different phases of the same original tumour. These tumours are at first surrounded by a capsule, usual sites being the upper or lower poles. With the growth of the tumour a general renal enlargement is noticed and later a lobulated surface can be felt. It sooner or later begins to infiltrate and finally invades the renal pelvis. It has a characteristic tendency to grow along the renal veins into the inferior vena cava.

The fact that lipoid material is a normal component of renal cells, the presence lumina or cysts and papillary in growth in these tumours, supports the view that they are only malignant nephromas.

Some, however, consider that there is a distinct group characterised by absence of reticulum and fibrous tissue which gives a better prognosis than the cancerous group after nephrectomy.

Metastasis first occurs in the lungs (44 per cent), then the liver (20 per cent), lymph glands and bones (8 per cent).

**Macroscopic Appearances.**—The tumour is most frequent in the upper and lower poles, lying under the capsule and sometimes in the central part projecting into the renal hilum. The tumour is at first globular in shape surrounded by a fibrous capsule of varying thickness and compressing the adjacent renal tissue. The surface presents a mottled, lobulated or mosaic appearance and divided into lobules by fibrous septa. Areas of hæmorrhages—some fresh, others old and organising, with areas of necrosis and gelatinous degeneration—are seen. The growth gradually extends into the calyces or gradually distends the kidney or forms a rounded projection near the poles and later infiltrates into perirenal fat and becomes adherent to liver, colon or diaphragm.

Carcinoma of kidney arises from renal epithelium. All carcinomas are uniformly firm in consistency, yellowish-white in colour and non-lobulated. The cells may be clear or granular and may be arranged in solid groups or as papillary adeno-carcinoma. Three types may be noticed:—

1. A diffuse infiltrating tumour, the cells being arranged in an irregular manner supported by dense fibrous stroma. The microscopic appearance resembles more a chronic inflammatory condition rather than a new growth.

2. *Papillary Adeno-carcinoma*.—This type is not uncommon. The cells are large, extremely clear with small, deeply staining nuclei. They are arranged on a delicate connective tissue and project into tubular spaces lined by the same type of cell. These have been mistaken for hypernephromas. But the cells in these are larger and clearer and a true hypernephroma should show no lumina formation.

3. *Alveolar Adenocarcinoma*.—The tumour resembles normal kidney tissue. The tubules, well formed but irregular, are found together with acini lined by cubical cells with granular protoplasm.

Most of the hypernephromas are either papillary or alveolar adenocarcinomas. A true hypernephroma should show no lumen formation and the scantiest of reticulum and should give rise to intensification of sex characters.

*Symptoms*.—The cardinal symptoms of new growths of the kidney are hæmaturia and tumour. Hæmaturia is present in over 90 per cent of the cases and is the initial symptom in 70 per cent. It may be intermittent and capricious. It lasts for a few days and disappears to reappear

after a few weeks or months. The blood is well mixed with urine and may be dark purple, or bright red, or only a pink tinge. When urine appears clear, it may show red blood cells under the microscope. The clots are thin, rounded and worm-like. Israel says that the clots in new growths of kidney are of the size and shape of maggots, are red, pale yellow, or white and are contracted at parts. They occur in a slightly bloody urine. Clots may block the ureter and give rise to ureteral colic with sudden subsidence of blood in the urine sometimes the bladder may fill rapidly with blood clots and cause strangery. Hæmaturia has no relation to the size of the growth. A small growth may cause as much hæmorrhage as a large one. It is due to the growth extending into the calyces or renal pelvis.

Pain in some form is usually present. It occurs as ureteral colic in about 46 per cent. during the passage of clots and as diffuse pain in the renal region in about 40 per cent. An aching renal pain may be due to tension within the renal capsule caused by engorgement of the kidney or hæmorrhage into the growth. Constant aching pain unaffected by movement or variations in hæmaturia and only temporarily relieved by drugs is the characteristic pain of renal cancer. It is due to spread of cancer and involvement of nerves. It may radiate into the genital glands, groin or down the thigh as sciatica when metastatic growths occur in the vertebræ.

Tumour is a very frequent sign being present in advanced stages in 84 per cent. It is usually noticed later than hæmaturia in malignant nephromas, unlike in embryomas in children where tumour formation is the first sign.

In growths of lower pole, tumour can be felt much earlier. A large growth is easily felt. It forms a rounded mass in the loin which is dull to percussion and feels solid. The colon may be rolled under the finger on the surface of the tumour or gives a resonant band crossing the tumour vertically. The tumour is rounded, firm, resistant and often smooth. When small, a sensation of ballotment may be detected by projecting it forwards against the flat of the hand on the abdomen. The tumour usually moves with respiration but it becomes fixed from infiltration into peri-renal tissue.

*Urine*.—In addition to the presence of blood and worm-like clots, it may occasionally show pieces of growth or cancer cells. Pyuria may be occasionally seen if calculus is also present. Polyuria may occur due to high pressure on the renal vessels.

Tests show an impaired renal function in the early stages.

Varicocele is sometimes seen. It develops steadily. It is often late in onset but sometimes may be seen early. It is due to pressure of the tumour or enlarged glands. It may be due to engorge-

ment of capsular veins which anastomose with spermatic vein. If the varicocele does not subside in the genupectoral position, it is probably due to enlarged glands and the case will be inoperable. Cachexia occurs in late stages, due to the anaemia, constant pain and neuralgia and want of sleep, etc.

Hypertrophy of left ventricle and increased arterial tension have been noted by some, and an abnormally rapid pulse may occur due to pressure on the lumbar sympathetic ganglia.

Roentgenograms show a dense shadow with an indefinite outline in large growths of the kidney. Metastatic nodules in the lungs and bones are clearly seen in X-ray pictures and this method of examination should be done prior to operations. Symptoms of pulmonary metastases may be insignificant.

*Course and Prognosis*.—Symptoms may be present for a number of years before patients submit themselves for operation. Some may come only after metastases into lungs and bones have occurred. The average duration of life after the appearance of symptoms is about four years. But when metastases have occurred the course is rapid.

*Diagnosis*.—The early diagnosis of renal growths almost entirely rests on cystoscopy and retrograde pyelography.

Braesch tabulates the changes noted in the outline of renal

pelvis and calyces in the presence of a new growth as follows:

1. Elongation of one or more calyces or of the pelvis.
2. Encroachment on the pelvic lumen causing flattening of pelvic outline, narrowing of individual calyces or complete occlusion.
3. Secondary pyelectasis.
4. Abnormal position and shape of renal pelvis.
5. Deformity at the pelvi-ureteric juncture and upper part of ureter.

The earliest deformity is one of elongation of one or more calyces with a distinct narrowing of the lumen giving "the spider leg" deformity characteristic of a new growth. If the tumour involves the pelvis extensively, partial or even almost complete obliteration of pelvis giving a shadow with more or less irregular edge with dilatation of some of the calyces may be seen. Where the tumour presses on the ureter there may be dilatation of one or more calyces or a general pyelectasis.

Similar deformities may be noted in polycystic kidney but the condition is bilateral and the deformities and defects show characteristic crescentic shapes from the pressure of cysts.

*Treatment.*—Total nephrectomy should be done as early as possible.

Contraindications for nephrectomy are:—

1. where growth has spread into peri-renal tissue and eradication is impossible;
2. where the opposite kidney is functionally inadequate;
3. where patient is weak and cachectic;
4. where the heart is dilated and feeble; and
5. where metastases are evident as seen by X-ray of lungs, etc.

In the case of large tumours a preliminary course of deep X-ray therapy may render the case fit for exploration.

In the case of large tumours transperitoneal exposure is the best as it permits of examination of lymph glands, and peritoneum covering the tumour for signs of infiltration and examination of liver for secondaries. It also allows an early ligature of the vascular pedicle which renders the subsequent steps of operation much easier.

In favourable cases, not only the kidney with the growth, but the peri-renal fat, the lymphatic glands and the supra-renal capsule are removed. This may be followed by a few deep X-ray exposures.

The mortality in selected cases is about 20 to 25 per cent.

*Late Results.*—Recurrence takes place in 60 per cent of cases, 70 per cent occurring in the first

year after operation after which it becomes less and is very rare after the fourth year. 7 to 10 per cent survive beyond four years without recurrence.

### Tumours of the Renal Pelvis and Ureter.

Growths arising in the renal pelvis itself are comparatively rare, forming about 7 to 8 per cent of renal tumours.

They may be divided into two main groups:—The papillary and the solid growths. The papillary group may consist of benign papillomas and papillary carcinomas. The solid group may be transitional-cell carcinoma or squamous-cell carcinoma.

Papillary tumours form 75 per cent of the growths. They seem to be more common in men than women. Papillomas are found in the fourth and fifth decades and the malignant growths in the fifth and sixth decades of life.

*Etiology.*—No predisposing cause has been found for papillary growths but presence of calculus and infection are important factors in the case of cancerous growths. More than 50 per cent of squamous-celled cancers have been found in conjunction with calculous pyonephrosis.

*Pathology.*—Papillomas are usually situated at the pelvi-ureteric junction. These may also be found in the ureter especially at its lower end and also in the bladder. The structure and appearance are similar to papilloma

of bladder but they show a greater tendency to become malignant. All papillomas sooner or later end as papillary carcinomas. These spread to the kidney and also along the ureter. When benign the papillae are fine and branched and are lined by epithelium of the same thickness and with definite layers as the normal pelvis, consisting of basal layer of cuboidal cells, a middle layer of fusiform cells and a superficial layer of squamous cells without cornification. The nuclei are regular in shape without any mitotic figures. The papillae show no tendency to fuse, nor is there any sign of infiltration of subjacent tissue.

*The Villous Type.*—Has very slender papillae springing directly from the mucosa like a tuft of grass, and may vary in length. They are made of a loop of capillaries surrounded by fine fibrous tissue and covered by transitional epithelium. They are friable and bleed profusely.

*Papillary Type.*—In this the papillae are short, unbranched and arise from a more or less well formed pedicle. The pedicle is long enough for the mass to be moved over the mucosa.

Malignant change is the rule in both types but earlier in the papillary-type. The growth may become extensive filling the whole of the pelvis and also spread down the ureter.

Papillary carcinoma arises from papilloma which proceeds to infiltrate the submucosa and then invades the renal tissue.

The pelvic growth may subsequently appear stunted.

Columnar-celled carcinoma forms a nodular growth. Prolonged inflammation of the renal pelvis or ureter causes transformation of the epithelium into stratified squamous epithelium and leuco-plakic patches are produced. From these squamous-celled epithelioma may arise. These tumours spread to adjacent structures and produce metastases. This growth is often fibrotic and hard and may cause dilatation of calyces.

*Symptoms.*—Hæmaturia is as common as in growths of the kidney. Intense renal and ureteral colic, accompanied by retention and distension of kidney occur. Variations in the size of kidney is very characteristic. On cystoscopy a tumour may be seen projecting from the ureter or implanted on the tip of the orifice. Catheterisation may show an accumulation of blood and urine in the renal pelvis. Cells characteristic of the growth may be found in the fluid. Fragments of growths may be passed in the urine following attacks of ureteric colic. A retrograde pyelogram may show filling defect in the outline of pelvis and calyces. Sometimes a hydronephrosis is seen due to partial obstruction by growths. In cases of solid growths pycelography may show only a diffuse infiltration of the walls of the ureter giving its lumen an exceedingly irregular appearance.

*Prognosis.*—Even in innocent papillomas prognosis is bad as they become malignant.

*Treatment.*—The treatment of villous tumours consists of nephro-ureterectomy. Where there is a tumour at the lower end of ureter, the bladder wall surrounding the ureter has to be also excised. Complete ureterectomy with nephrectomy is often required.

#### Peri-renal Tumours.

These are rare, but present a large variety of structures. Some develop from vestigial remains around the kidney, some arise in the renal capsule and others arise in the retro-peritoneal tissue and their relation to the kidney is accidental.

They may be solid or cystic. Of the solid tumours, lipomas are more frequent than others. These may be pure lipomas, fibro-lipomas, myxo-lipomas or fibro-myxo-lipomas. Fibromas or fibro-myomas containing non-striped muscle fibres may be found in relation to the fibrous renal capsule. They are usually small and rarely attain a large size. The fibro-lipomas may show areas of calcification and give a puzzling appearance in radiograms.

Sarcomas, fibrosarcomas and angiosarcomas may occur. These become adherent to neighbouring structure very early.

Mixed tumours are rare, and resemble those of the kidney. They arise in remains of Wolffian body.

Cysts may be unilocular or multilocular. The unilocular

#### Neoplasms of the Kidney

types contain clear yellow fluid in which urea and uric acid may sometimes be seen. Polycystic tumours may occasionally occur.

The cystic tumours are believed to arise in the remains of Wolffian body or from inclusions of embryonal peritoneum in perirenal tissues.

When they arise from the fibrous capsule of kidney they are firmly adherent to the kidney. Those arising in the fatty capsule are not adherent, but the organ becomes buried in the growth. Atrophy from pressure and obstruction of ureter may occur. Sarcomas become early and densely adherent to peritoneum and intestines. Necrosis with pseudo-cyst formation and calcification may occur in the solid tumours. The bulk of the tumour may be lateral or medial to the colon. Cysts rarely form adhesions to surrounding structures.

*Symptoms.*—Presence of a tumour in the loin with the colon in front, usually of irregular contour and slow growth except when sarcomatous. Pain may be present. Varicocele, constipation, ascites and œdema may occur from pressure on the veins. Urine is normal. The tumour may give firm, soft or cystic feel according to its consistency.

*Diagnosis.*—Help in this may be obtained by ascending pyelogram which may show the relationship of tumour to the kidney and ureter.

*Treatment.*—The growth should be removed in the early stages. For small growths the lumbar route is chosen, but for large one the transperitoneal route is safer. If possible the kidney should be saved but in a large number, it may have to be sacrificed.

## Clinical Memoranda.

### TWO CASES OF EXTENDED BREECH IN A PRIMIPARA.

BY R. G. KRISHNAN, F.R.C.S.,

*Government Hospital for Women and Children, Madras.*

CASE I. Lokamma, aged 17, a primi, with a history of nine months' amenorrhoea, was admitted on 12th March 1938 for headache and oedema of both legs. She had the symptoms for ten days.

Examination at the time revealed an anæmic ill-nourished woman with moderate oedema of both legs and feet. Heart sound in the pulmonary area was soft. Abdominal examination revealed the uterus enlarged to full term with the foetus presenting by the breech. Feet were felt near the head. Uterus was not acting and the foetal heart rate was 136. Urine was clear and blood pressure 115/75.

Her pelvic measurements were I. C. 9½", I. S. 8½", and E. C. 6¾".

She was put on large doses of iron, calcium lactas, marmite and intravenous injections of hypertonic glucose.

On 17th March 1938 at 6 p.m. she was found to be suffering from hurried respiration with a pulse rate of 80. Nothing was found in her lungs or heart to account for the dyspnoea. She was given an injection of camphor in oil.

Her bladder was distended, her uterus was contracted and tense rising up beyond the level of the costal margin and deflected to the right. She was thought to have had hydramnios with pressure symptoms causing dispnoea.

On 18th March 1938 she was having slight dyspnoea and complaining of headache and blurring of vision. Her face was puffy, oedema of the feet was persisting in spite of restriction of diet and treatment. At 12 noon her membranes were ruptured artificially. At 6-15 p.m. vaginal examination showed the cervix high up with the os about 1½ dilated with the buttocks presenting. At 9 p.m. there was the same dilatation of the os.

On 19th March 1938 os was fully dilated. Under general anaesthesia both feet were brought down and as the cord was not pulsating the foetus was extracted deeply asphyxiated. The child was revived by the usual means.

CASE II. Pushpavathi, aged 18, a primi, with a history of nine months' amenorrhoea, was admitted on 12th March 1938 at 10 a.m. with labour pains. Examination at the time showed a well-built

big woman. Abdominal examination revealed the uterus enlarged to full term with the foetus presenting by the breech. The lie was oblique. Feet were felt near the head. Uterus was acting and the foetal heart rate was 144. Urine was clear and blood pressure 120/80. Her pelvic measurements were I. C. 10¾", I. S. 9" and E. C. 7¼".

She was seen by the First Obstetrician who ordered a tight binder to be applied to abdomen and a foot to be brought down when the os was fully dilated. Though the lie was oblique the breech was palpated in the right iliac fossa. It was therefore thought that the lie might become vertical when she got strong pains. She not being an elderly primi, Caesarean section was not considered necessary.

2 a.m.—Membranes ruptured. Vaginal examination showed the

os 4/5 dilated and frank breech presenting. Under general anaesthesia a foot was brought down without difficulty.

2-35 a.m.—The child was extracted as the cord was found not pulsating, in an asphyxiated condition. It was revived with the usual treatment.

3-5 a.m.—The placenta was expressed and she had post-partum hæmorrhage first degree.

On 16th March 1938 lochia was offensive without any rise of temperature. On 18th March 1938 she and her baby were discharged well.

My thanks are due to the Superintendent, Government Hospital for Woman and Children, Egmore, for his permission to publish these cases.

### TWO CASES OF SUSPECTED ECTOPIC PREGNANCY.

BY DR. R. G. KRISHNAN, F.R.C.S.,

*Government Hospital for Women and Children, Egmore, Madras.*

#### 1. A Case of Acute Appendicitis complicating Pregnancy.

This should be regarded as a very serious complication as many women die, if not operated upon; while the surgical procedures undertaken for its relief are frequently followed by premature labour as in this case.

The patient was a 22-year-old first para. Her previous history

showed nothing of interest. The patient gave a history of two months' amenorrhoea. Her present history began a week earlier with loss of appetite. She got a severe and sudden pain in the abdomen round about the umbilicus the previous day of her admission into this hospital on 10th December 1937. She vomited once after the onset of the pains. She had no bleeding per vaginam.

Examination at the time showed a short well-nourished woman with an anxious expression. Her general condition was good. Her temperature was 99.4°, pulse rate 94 and blood pressure 100/60. Urine showed nothing abnormal. W. B. C. 9,000. The abdominal examination disclosed tenderness and rigidity over the whole lower abdomen but marked over the right iliac fossa. There was no free fluid or impaired note of resonance in the flanks.

Vaginal examination showed a soft cervix and a soft tender mass in the right fornix. Body of the uterus could not be made out. There was no blood on examining finger. She was seen by the First Obstetrician. She was suspected to be a case of ectopic pregnancy. Operation was decided upon and arrangements made to get the permission of her husband. At 1.30 p.m. her pulse went up to 120. When her abdomen was opened under general anaesthesia, uterus was found enlarged to about six weeks' size, soft and pregnant. Tubes and ovaries were normal. Appendix was bound down by adhesions and kinked in its middle third. Adhesions were freed and appendix removed.

Her immediate post-operative reaction was satisfactory till the 17th when she began to bleed per vaginum. Vaginal examination revealed an inevitable abortion. On 23rd December 1937 her uterus was evacuated. She was discharged cured 13th January.

## 2. A Case of Twisted Dermoid Cyst of Ovary complicating Pregnancy.

This condition is rarely come across. Out of 107 cases of tumours complicating pregnancy collected by McKerran, 46 were dermoid cysts.

The patient was a 33-year-old third para. Her previous history showed nothing of interest. She gave a history of seven weeks' amenorrhoea. Her present history began eight hours before admission into this hospital on 16th December 1937 when she got a severe and sudden pain in the right lower abdomen. It was continuous and increasing periodically. There was no bleeding per vaginum. She vomited once after the onset of pain.

Examination at the time showed a well-built woman with a tongue slightly coated and moist. Her general condition was good. Her temperature was 98.4°, pulse 92 and blood pressure 120/80. Urine showed a few pus cells in the centrifuged deposit. B.C. 13,750.

The abdominal examination disclosed no rigidity of the abdominal muscles. Tenderness was present in the right iliac fossa, below McBurney's point. A tender mass was felt rising from the pelvis on the right side.

Vaginal examination showed a soft cervix with the external os open. Body of uterus was found enlarged to about ten weeks' size. A soft swelling was felt in the

right fornix which was continuous with the swelling felt per abdomen. No blood on examining finger. Left fornix was clear. She was seen by the First Obstetrician. She was thought to be a case of ectopic pregnancy and operation was decided upon.

Next day her abdomen was opened under spinal anaesthesia. The right ovary was enlarged in size and shape like a kidney, dark and congested and twisted in the region of the meso-salpinx; the right tube and meso-salpinx congested and thick. They were removed. The body of the uterus was enlarged to ten weeks. Abdomen was closed in layers.

On section the specimen showed a cyst with sebaceous material in the middle of the ovary.

Her immediate post-operative reaction was satisfactory. She did not abort. She was discharged cured on 6th January 1938.

Her pregnancy continued to term and a normal healthy child was delivered naturally in this hospital.

*Comment.*--Both the cases were suspected to be ectopic pregnancy as their history, symptoms and signs found on abdominal and vaginal examinations were strongly suggestive of ectopic pregnancy. The first proved to be a case of acute appendicitis and the second dermoid cyst of the ovary with a twisted pedicle.

The mistake in the pre-operative diagnosis in these cases did not matter as the treatment in these cases is immediate laparotomy.

In conclusion, my thanks are due to the Superintendent, Government Hospital for Women and Children, Egmore, for permission to publish these cases.

## Gleanings from Current Medical Literature.

### MEDICINE AND THERAPEUTICS.

**Tropical Macrocytic Anæmia: Its Relation to Pernicious Anæmia.** LUCY WILLS and BARBARA EVANS (*Lancet*, August, 20, 1938). Tropical macrocytic anæmia does not respond to the more highly purified liver extracts, which contain the liver principle curative in pernicious anæmia in relatively pure form.

This fact further differentiates this disease from pernicious anæmia and demonstrates the presence of a new hæmopoietic factor in crude liver and autolysed yeast extracts.

This factor is almost certainly identical with the one described in the production and cure of the nutritional anæmia (macrocytic) of monkeys; it is not vitamin B<sub>1</sub>, B<sub>6</sub>, lactoflavin, or nicotinic acid but has not yet been separated from the yeast-fuller's earth filtrate of Edgar and Macræ.

For the treatment of tropical macrocytic anæmia crude liver or autolysed yeast extracts should be used.

**Therapeutics of Cobra Venom.** D. I. MACHT (*Ann. of Inter. Med.* [1938], 11, 1824) states that cobra venom, like opium and its principal alkaloid, morphine, relieves pain through its action on

the higher centres of the brain. While morphine relieves pain promptly and the effect wears off within a few hours, cobra venom does not induce analgesia rapidly, but once it is induced the analgesia lasts much longer than that of morphine. Once analgesia has been established, patients may usually be kept comfortable with two or three weekly intramuscular injections of 5 mouse units of cobra venom. The author has personally administered two such injections twice a week to patients with advanced and hopelessly malignant cancers for months in succession and he has been able to keep them comfortable without using any other drug. The author has extended the use of cobra venom to the treatment of certain non-malignant conditions (severe neuralgias, chronic arthritis and angina pectoris with subacute, long-lasting paroxysms of pain). The number of arthritic cases treated with this agent is still not large enough to warrant discussion, although considerable relief of pain has been obtained in some instances. Cobra venom has also relieved the pain, relaxed the rigidity of the muscles and produced a general amelioration of parkinsonian symptoms in seven cases.

**The Antidotal Treatment of Barbiturate Intoxication: Report of Treatment with Picrotoxin.** W. J. BLECKWENN and M. G.

MASTEN (*J.A.M.A.*, August 6, 1938). The use of picrotoxin as an antidote is based on the work of Tatum and others who showed that in the dog 1 mg. of picrotoxin acts as antidote for 35 mg. of amytal, 36 mg. of pentocton and 27.7 mg. of pentobarbital sodium. While from 2 to 4 mg. of picrotoxin per kilogram was fatal to rabbits, when protected by adequate doses of barbitals 20 to 40 mg. per kilogram could be tolerated. Human observations were made as follows: With a 5 per cent solution of the various short acting barbiturates, the patient was narcotised to the point of corneal anaesthesia. After an interval of 10 minutes to make sure that the necessary depth of anaesthesia had been established, picrotoxin in a 1 in 1000 solution was injected at the rate of 1 c.c. per minute. The return of the corneal reflex and the dilatation of the miotic pupil were warnings of approaching consciousness. A few milligrams more brought the patient round to full consciousness. It was thus deduced that 1 mg. of picrotoxin was antidotal to about 30 to 40 mg. of the short acting barbiturates.

In any case of deep coma ascribable to barbiturates the following line of treatment may be adopted:—The first step should be to wash out the stomach. Since the drug may be absorbed anywhere in the gut, rapid peristalsis and elimination may be accelerated by leaving 2 or 3 ounces of sodium phosphate in the stomach after the last washing. To overcome the anoxia and

cerebral anæmia continuous oxygen inhalation should be given by a nasopharyngeal catheter. Diuresis is promoted by parenteral injections of fluids and dextrose. Picrotoxin is given in a 1 in 1000 solution at the rate of 1 c.c. per minute, watching the pupils and taking the corneal reflex at intervals. The first notable effect will be an increase in the depth of respiration and a rise in blood pressure. The return of corneal and other reflexes and twitchings are signs that the convulsive stage is approaching. Patients who show evidence of having passed from deep anaesthesia to a lighter plane after picrotoxin but who remain unconscious are in a safe stage and unconsciousness is probably due to cerebral oedema from which recovery may be hastened by diuresis. Picrotoxin appears to stimulate the medullary and perhaps the hypothalamic centres even in those cases in which unconsciousness cannot be restored because of cortical anoxæmia and oedema.

Picrotoxin is also known to protect animals against chloral hydrate, paraldehyde and sodium bromide.

**The treatment of Parathyroid Tetany with Dihydro-tachysterol.** C. M. MACBRYDE (*J. A. M. A.*, Vol. III, July 23, 1938). A derivative of irradiated ergosterol known as dihydro-tachysterol (which is an isomer of ergosterol like calciferol) has been found to raise blood calcium and with small doses given orally, it has been found possible to maintain patients with tetany symptom

free and to keep the blood calcium at normal level. The substance has been employed in an oily solvent containing 5 mg. per mil.  $\frac{1}{2}$  mil. is given *t. d. s.* and after the blood calcium level reaches the normal height the dose is reduced to  $\frac{1}{2}$  mil. per day. Dihydro-tachysterol has certain very definite advantage over parathyroid extract in the treatment of chronic tetany. The effect is more prolonged, it can be given orally, no tolerance is developed, it is less expensive than parathyroid and it is stable and retains its potency when kept at ordinary room temperature. Small doses of calcium salts given along with dihydro-tachysterol cause remarkable and prompt rise in blood calcium. The mode of action is yet to be studied. Indiscriminate use cause hyper-calcaemia and severe toxic effects. Large doses given to experimental animals have caused decalcification of the bones and metastatic calcification.

**Climatic Bubo or Lymphogranuloma Inguinale.** H. M. HANSCH (Trans Roy. Soc. Trop. Med. and Hyg. 1938, V. 31, 578-84—Abst. Bull. Hyg.) [The author described his experience of 130 cases of lymphogranuloma inguinale occurring out of a total of 17,000 male cases at the Seamen's hospital. All the infections occurred in the tropics or sub-tropics and therefore it would appear that indigenous infection in Britain must be very rare. In only four cases was a primary lesion seen and only two of the cases of lymphogranuloma inguinale occurred in circum-

### The Madras Medical Journal

cised men, which suggests that the prepuce is nearly always the site of infection. Differential diagnosis from syphilis is usually easy by means of the dark ground microscope or serum tests and from chancroidal bubo by reason of the fact that lymphogranuloma inguinale buboes show more peri-adenitis, less pain, more fever and less suppuration, whilst the Frei and Dmelcos intradermal tests are most valuable, though it must be admitted that different samples of Frei antigen vary considerably.

**Treatment.**—Rest in bed will often cause rapid subsidence of the bubo; if there is fluctuation the pus should be aspirated and the puncture sealed. Intravenous T. A. B. vaccine often hastens resolution of the adenitis and 85 per cent of cases can be discharged in 4 to 6 weeks. In the remaining 15 per cent excision of the affected glands will generally hasten recovery.

**The Control of Meningococcic Meningitis Epidemics by Active Immunisation with Meningococcus Soluble Toxin—Further Studies,** KUHGS. D. M. KISNER P. WILLIAMS, M. P. and MOORMAN PEARL (J. A. M. A. 1938, V. 110, 484-87). Of 7,339 cadets in 48 different camps in Missouri tested intradermally with 0.1 c.c. of a 1 in 200 dilution of the soluble toxin in the filtrate from Meningococcus broth culture, 3,926 or 53.5 per cent showed a one *plus* or greater reaction: 3,717 of the original positive reactors were retested after an interval of approximately two months, and the reaction of

78.9 per cent had changed from positive to plus minus or negative.

All cadets with a one plus or greater reaction were inoculated with 0.5, 1 and 1.5 c.c. of full strength filtrate at four day intervals. The greatest reactions were caused by the third dose. This dose produced mild systemic reactions with temperatures occasionally at 101° or 102° F. No untoward reactions occurred.

One month after this immunisation three cadets in three different camps who had not been immunised developed meningococcic meningitis. No case occurred among those immunised in the seven winter months following inoculation. Prior to giving the toxin there were nine outbreaks of one case each.

In immunising newly concentrated groups in the presence of impending epidemics the authors consider that the safest procedure is not to depend on the intradermal test to differentiate the immune from the non-immune, but to inoculate the entire group (Abst. Bull. Hyg.)

### SURGERY.

**The Therapeutic Value of Glycerol Trinitrate in Biliary Colic and in the post operative phase of Biliary Tract Disease,** BEST, R. R. and HICKEN, N. F. (Am. J. Surg. 1938, 39, 533, Abst Surg. Gynaec. Obst).

The histological study of the extra-hepatic biliary system revealed more abundant muscle tissue in the fundus and neck of

the gall bladder wall than at the site where the cystic duct approached the common bile duct. The so-called 'Collum cysticus' sphincter was not identified. The hepatic and common bile ducts consisted mainly of fibro-elastic tissue with scattered strands of muscle tissue down to the region of the ampulla and the sphincter of oddi where non-striped muscle again appeared and reached its maximum thickness. It formed a sphincter which mechanically guarded the entrance into the duodenum and which clinically induced a typical sphincteric syndrome.

Atropine, morphine and atropine, epinephrine, ephedrine, magnesium sulphate, and fats, such as cream or olive oil, were found to be effective, either individually or in combination, in relieving only a small percentage of cases.

Nitroglycerin was given to three groups of cases.

1. In ordinary biliary colic when the gall bladder had not been removed nitroglycerin gave relief in some cases and was a failure in others.

2. In the cases of patients whose gall bladder had been removed some years previously but who still had attacks of biliary distress, the drug gave immediate relief when other antispasmodics had failed. With the use of this drug, it was noted that small stones were released from the common bile duct, there being no relief if the stones were too large to get through the chole-

dochus sphincter or were caught in a narrowed portion of the common duct.

3. In cases of patients with spastic biliary dys-synergia, who were carrying common duct tubes or catheters and in whom the distress was caused by a disturbance of the sphincter of oddi, glyceryl trinitrate often brought about immediate cessation of pain when the combination of morphine and atropine had not given the desired relief. Nitroglycerin may be used in combination with morphine, as the relaxing effect of the nitroglycerin on the sphincter seems to be greater than the spastic effect of morphine on the duodenal wall. Atropine seems to give the most relief if the gall bladder and cystic duct are involved. When there is an active pathological condition, atropine or a combination of morphine and atropine was not always successful. The greatest success with the use of glyceryl trinitrate has been obtained in those cases in which rather typical distress recurred following the removal of the gall bladder.

### OBSTETRICS.

**Aetiology of Eclampsia** W. PATTERSON, H. HUNT and R. NICODEMUS (*Am. J. Clin. Path.*, 1938, 8, 120-135). Pregnant rabbits, unlike women, developed a hypocholesteræmia in the last two-thirds of pregnancy. Total thyroidectomy produced a hypercholesteræmia in the non-pregnant rabbit. The blood cholesterol of foetuses of total thyroidectomised rabbits was over 100 per cent higher than in fo-

tuses of normal rabbits; the thyroid glands of the former group showed marked hyperplasia. The thyroidectomised rabbits died in convulsions shortly before term with toxic hepatitis and nephritis and infarcted placenta with severe endarteritis of the placental arteries. It was concluded that the foetal hypercholesteræmia causes placental infarction. Eclampsia has a physiological and pathological basis identical with the syndrome in pregnant thyroidectomised rabbits. Administration of thyroid extracts lowers the human hypercholesteræmia in the last two trimesters of pregnancy and thus there must be a subclinical hypothyroidism present. Maternal hypothyroidism plus hypercholesteræmia causes foetal hypothyroidism and hypercholesteræmia which may lead to placental infarction. Toxins absorbed from the degenerating placenta produce changes in the maternal organs. (*Abst., Brit. Chem. Phys. Abst.*)

**Experimental Interruption of Pregnancy.** (*B.M.J.*, September 10, 1938: Editorial). The clinician at present has at his disposal only such oestrogenic preparations as are derived from natural sources, namely, oestradiol, the hormone actually secreted by the follicle and its two degradation compounds, oestrone and oestriol. The scope of activity of these compounds is fairly well defined. The atrophic uterus of amenorrhoea may be restored to normal dimensions and oestrin withdrawal bleeding induced. Spasmodic dysmenorrhoea, uterine inertia and

atrophic vaginitis may all be successfully treated, but injection of the material is usually required. Oral effectiveness is limited to the relief of menopausal symptoms. The principal measures introduced to prolong the effect of the injected hormone are esterification of the hormone with benzoic acid and the subcutaneous implantation of the tablets of the pure crystalline material. The latter has been found to produce an oestrogenic effect which may last from six weeks to three months. Progesterone and testosterone have been for some time available in synthetic form. Oestradiol and its derivatives on the other hand have not been synthesised. During the past year or so however synthetic compounds have been prepared which show oestrogenic properties to a varying extent. These compounds, it should be emphasised, bear little relation chemically to the naturally occurring sex hormones, which are cyclo-pentano-phananthrene derivatives. One such synthetic compound with potent oestrogenic properties has been prepared by Dodd and his colleague—*diethyl stilboestrol*, a derivative of the relatively simple aromatic substance stilbene. It is highly active by mouth and can induce a number of oestrogenic effects. The fact that it is chemically unrelated to oestrin, however, makes it possible that its effects may not exactly correspond either quantitatively or qualitatively to those of the naturally occurring hormone. In the current issue of the Journal Parkes, Dodds and Nobel report on the

potent anti-progesterone effect of the oral administration of this synthetic compound, which is capable of preventing nidation of the fertilised ovum and of causing interruption of established pregnancy in experimental animals. The application of this work to the human female may open up the most important possibilities and it seems likely that hormonal prevention and termination of pregnancy are within sight, though a considerable amount of careful clinical investigation such as is being undertaken at the present moment, is needed before any definite statement can be made on this matter. The other substance investigated by Parkes, Dodds, and Nobel is *ethinyl-oestradiol*. The addition of the ethinyl group to the sex hormones has been found to increase their oral effectiveness very considerably. Ethinyl oestradiol, for instance, is seventeen times more effective by mouth than oestradiol. Ethinyl progesterone is also active by this route, though progesterone itself has to be injected to produce any result at all. Oral administration of ethinyl oestrogen appears to antagonise progesterone even more effectively than oral administration of diethyl-stilboestrol. The future application of these two compounds will be watched with much interest.

### VITAMINS.

**Absence of Nicotinic Acid from the urine of pellagrins: Its determination.** S. P. VILTER, T. D. SPIES and A. P. MATTHEWS (*J. Am. Chem. Soc.*, 1938, 60, 731). 0.1 to 1 mg. of nicotinic acid or

its amide is determined calorimetrically by treating 3 c.c. of decolorised urine first with 2: 4-dinitrochlorobenzene and then with NaOH. Pyridine and nicotine, methylated betaine, and trigonelline give similar colours, which are due to the *tert.* N. Normal urine gives this test, but not urine of pellagrins or of persons having subclinical pellagra in relapse, and the test thus has diagnostic value. Ability to give the colour is restored, if absent, by feeding nicotinic acid.

### THE VITAMIN-B COMPLEX.

(From the *British Medical Journal*, dated 17th September 1938.) Until about thirteen years ago Vitamin-B was regarded as one substance with two functions; it cured or prevented Beri-beri in man and Polyneuritis in pigeons, and it was necessary for the growth of rats. In many food substances tested the amount that had to be added to the Vitamin-B-deficit diet of the rats in order to make them grow bore a fairly constant ratio to the amount that was needed to cure a pigeon of polyneuritis, allowance being made even in those days for the variation in response to different animals to equal doses of the same substance. However, as details of experimental technique with animals came under more careful control it became evident that the ratio of the anti-beri-beri potency to the growth promoting potency in different substances varied widely. A substance which could cure polyneuritis in pigeons by a very small dose was not nearly

so potent in promoting growth in rats otherwise deprived of Vitamin-B. This was particularly evident in the Vitamin-B concentrates prepared by the method of Peters and his co-workers. The more potent his concentrates became in their anti-neuritic property the less effective were they in supplementing the Vitamin-B-deficient diets of rats. It was known at this time that by autoclaving yeast its anti-neuritic potency was destroyed and that it could not make good the deficiency of the rats' diets. Workers in several laboratories, however, soon showed that when anti-neuritic concentrates and autoclaved yeast were given to rats fed on the Vitamin-B-deficient diet the animals could grow. This, then, proved the existence of two factors at least in Vitamin-B, and they were tentatively named Vitamin-B<sub>1</sub> the anti-neuritic and more heat-stable constituent, and Vitamin-B<sub>2</sub> the more heat-stable constituent. In the U. S. A. some workers preferred to call these two factors B and G; others, F and G.

Further work revealed the existence of other factors which were water-soluble and therefore classified temporarily as B Vitamins. One factor present in wheat germ was found to be necessary for the maintenance of weight in pigeons and named Vitamin-B<sub>3</sub>. Another very heat-labile factor in yeast, necessary for the rat and chick, received the

name Vitamin-B<sub>4</sub>; another, necessary for the pigeon, was named B<sub>5</sub>; and another, necessary for the rat (anti-dermatitis), was named B<sub>6</sub>. Still another factor, present in liver extract, is regarded as preventing dermatitis in chickens; it is generally known as the "filtrate factor". It could not be determined which of these was the anti-pellagra factor, for none of them was obtainable in a pure form except Vitamin B<sub>1</sub>, which was completely ineffective in the treatment of pellagra. Further work on what had been called Vitamin B<sub>2</sub> demonstrated that the effects were due to two substances at least lactoflavin, known as riboflavin since its composition was determined and the anti-dermatitis factor, previously called Vitamin B<sub>3</sub>, which Lepkovsky has recently claimed to obtain in crystalline form but neither of these proved to be the pellagra-preventive factor. Less than twelve months ago, however, Elvehjem showed that nicotinic acid cured black tongue in dogs, a condition which is thought comparable with pellagra in man, and clinical trials have since proved that nicotinic acid can indeed cure the most typical symptoms in the pellagra syndrome. Carter and O'Brien have now confirmed the earlier findings of the pigeon's need for Vitamins B<sub>1</sub>, B<sub>2</sub>, B<sub>3</sub>, and riboflavin. Macrae declares that the rat requires Vitamin B<sub>1</sub>, lactoflavin, an unidentified factor present in an autoclaved

aqueous yeast extract with fuller's earth (yeast-filtrate factor), and an unidentified factor present in the barium hydroxide eluate of a fuller's earth adsorbate from an autoclaved aqueous yeast extract (yeast-eluate factor). Nicotinic acid was not either of these yeast factors. Amyl alcohol extracts prepared from liver extracts contained a growth factor for rats distinct from all the preceding ones. Thus the number of factors tentatively included in the term Vitamin-B complex is by no means clearly determined. Those whose existence is generally accepted at present are B<sub>1</sub> (aneurin or thiamine), lactoflavin (ribo-flavin), Vitamin B<sub>6</sub> (the rat anti-dermatitis factor), and nicotinic acid (the anti-pellagra factor). Others accepted by many workers are Vitamin B<sub>3</sub>, B<sub>4</sub>, B<sub>5</sub>, the liver filtrate factor, chick anti-dermatitis factor, and Macrae's yeast filtrate and yeast-eluate factors.

Returning to Vitamin B<sub>1</sub>, it may be recalled that Westenbrink showed that by feeding rats on a diet free from this all the tissues of the rats except the brain became depleted of their reserves of Vitamin B<sub>1</sub>, within five or six weeks. The amount stored in the tissues is limited by dependent on the intake. Excess is excreted in the urine. Harris and Long have stated that "a daily excretion of less than 12 International Units raises the presumption that the diet contains less than a normal allowance of

Vitamin B<sub>1</sub>". Babkin has demonstrated that the gastric glands of dogs on the Vitamin-B-deficient diet do not respond to the usual stimuli-sham feeding, subcutaneous injection of histamine, the presence of food or 5 per cent solution of alcohol in the intestine. When yeast was administered the responses became normal, but the effective substance in the yeast was not determined. These results may afford an explanation of the anorexia so characteristic of the Vitamin-B<sub>1</sub>-deficiency. Molitor and Sampson have found that Vitamin B<sub>1</sub> is without influence on the contractions of the intestine. The role of Vitamin B<sub>1</sub> in the metabolism of carbohydrate, fat, and protein is still a subject for experiment. Peters and his co-workers have postulated the theory that it acts as a co-enzyme in the metabolism of carbohydrate, more especially in the oxidative breakdown of pyruvic acid. This is supported by a large amount of experimental work on the ratio between oxygen uptake and disappearance of pyruvic acid in normal brain tissue and in brain tissue of pigeons suffering from the Vitamin-B<sub>1</sub>-deficiency. It is suggested by Lipmann that Vitamin B<sub>1</sub> is converted into Vitamin pyrophosphate by the brain tissue, and that in this form it acts as a co-ferment helping either the carboxylase to break down the pyruvic acid to acetaldehyde and carbon dioxide or the oxidase to oxidise the pyruvic acid to acetic acid and carbon dioxide.

Vitamin B<sub>1</sub> exerts a demonstrable action only with B<sub>1</sub>-deficient

animals. Excess dosage has no effect. No toxic symptoms have been observed when amounts 25,000 times the estimated daily requirement were administered. Hawes has obtained dramatic cures by giving large injections of Vitamin B<sub>1</sub> to patients suffering from acute fulminating cardiac beri-beri. Stern has injected synthetic vitamin B<sub>1</sub> in doses of 500 to 50,000 International Units intrathecally for the relief of intractable pain and for inflammatory and degenerative diseases of the central nervous system. The action of the vitamin is much quicker when injected than when given by mouth. Fischer determining the amount of Vitamin B<sub>1</sub> in the crystalline lens in cases of cataract, found less of it and more pyruvic acid than in the normal lens, and concluded that the vitamin plays an important part in the oxidation-reduction system of the lens. The question of the presence of Vitamin B<sub>1</sub> in white and wholemeal flours and breads has lately been reinvestigated by Copping and Roscoe. They found that straight-run white flour, whether new or old, bleached or unbleached, contained 0.37 International Unit per gramme. Patient flour contained none and wholemeal 1.18 units per gramme. Bread made with yeast had no more Vitamin B<sub>1</sub> than the flour from which it was made. Thus a man would have to eat each day more than half a pound of white bread made from straight-run flour—not from patent flour—in order to obtain about a quarter of the Vitamin B<sub>1</sub> needed. The importance of brown bread

or of wholemeal bread in the diet has been stressed already. biochemistry increases every year.

#### HOSPITAL MANAGEMENT.

Day, Darby and Cosgrave claim to have shown that riboflavin is the anti-cataract factor, but Morgan, Cook and Davison are of opinion that the filtrate factor was the anti-cataract factor. They believe that both flavin and Vitamin B<sub>6</sub> are produced, probably by micro-organisms, in the intestines of rats fed on large proportion of lactose, but this did not prevent the development of cataract in a large proportion of their rats. They found that the filtrate factor was in corn starch or was produced in the intestines when it was given in the diet. Carlsson and Sherman have demonstrated that the amount of riboflavin stored in the body depends on the diet of the animal. In well-nourished animals the concentration of riboflavin in the liver was ten times that in the skeletal muscles; the concentration in the kidney, brain, and spleen was intermediate between these extremes. Sobrell and Onstott have determined that the condition in dogs which they had previously described as "Yellow liver" is due to a lack of riboflavin and can be cured rapidly by early parenteral administration of that substance.

This survey of a number of the recent studies on the B-Vitamins gives some idea of the complexity of the work that is being carried out and also of the intensity of the attack of the bichemist on the multifarious problems presented to him. The debt of the clinical worker to

**The Voluntary system in Figures** (*British Medical Journal*, dated 2nd July 1938, Page 24). The voluntary hospitals are a long time dying. It might be argued that they are no longer voluntary in the sense of the words which are still to be seen over the entrances of many of them—"Supported by voluntary contributions"—for voluntary gifts in the shape of subscriptions, donations, congregational offertories, even including workmen's contributions, Hospital Saturday funds, and contributory schemes, amount in all to much less than half the income available for maintenance. But as Mr. R. H. P. Orde, editor of *The Hospitals Year-Book* points out in a foreward to the new edition, the reference to voluntary contributions has largely obscured the picture. The really important characteristics of the voluntary system are not the sources of income but the absence of statutory control and of the desire to make any profit out of the treatment of the sick.

With that definition in mind it is worth while examining some of the massive statistics presented in the year-book. They relate to 1936, the last year for which complete figures are available. During that year 1,378,050 patients were treated in the wards of the voluntary hospitals of Great Britain and Ireland, and 6,216,497 in their out-patient departments. These figures show

increases over the previous year of 52,614 in-patients and 272,544 out-patients. The growth of the out-patient department catches the eye everywhere in the procession of statistics. In the London hospitals alone the number of new out-patients in the year was just upon two million, an increase of 80,000 on the year before. At the twelve London hospitals associated with medical schools the new out-patients numbered well over three-quarters of a million. At two of them (the London and St. Thomas's) the number in each case was over 100,000. At this rate the out-patient clinics will vie with the cinema as the place of resort for the British people. The same story is repeated at the special hospitals. At the four large ophthalmic hospitals in London, for example, the new out-patients numbered 72,000. The cost of out-patients is rather difficult to assess, and the disparity of some of the figures in the analyses suggests that different methods are taken by different hospitals. At the Birmingham General Hospital, for example, the remarkable figure of 6s. 8d. is returned as the cost per out-patient attendance, but in general at the provincial teaching hospitals the figure works out at something over one shilling, and at the London teaching hospitals, it averages just over two shillings.

An interesting section of the report this year deals with hospital nurses. In the London hospitals associated with medical schools the number of beds per member of nursing staff varies

from 2.46 at St. Mary's to 1.34 at Guy's, and at similar hospitals elsewhere in the country from 3.05 at Aberdeen Royal Infirmary to 1.97 at Addenbrooke's Hospital, Cambridge. Very few hospitals, whatever their size, have more than four beds per member of nursing staff. The average for the 800 hospitals furnishing complete particulars on this point is 2.36 in the case of the general hospitals and 2.84 in the case of the special, the special including such places as Spa hospitals, where the number of beds per nurse may be from ten to fifteen. On a summary of information from a number of large provincial hospitals the number of hours' duty per week for the day staff (excluding times taken for meals) is about fifty-five, and for the night staff very generally over sixty. Typical salaries for matrons of large provincial hospitals are £400, for ward sisters £90—£150, for staff nurses £60—£80, and for fourth-year probationers £40.

The financial position of the voluntary hospitals in 1936 may be summarised by saying that they received £17,680,000 and spent £17,167,000. Returning prosperity to the nation brought the hospitals a welcome increase in voluntary gifts, the total of which was £6,071,000, a gain of not far short of £300,000 on the year. The only diminution was in Scotland. But the cost of running hospitals is generally rising, reflecting the rising price level, and the fear of a deficit is ever present in the minds of hospital managers. An independent view of the whole situation

was put forward the other day by Professor Ernest Barker, who holds the chair of political science at Cambridge, in an address to the British Hospitals Association on "The State and the Voluntary Hospitals". The deficits of the hospitals, said Professor Barker, were in no sense the result of bad management. Hospitals had developed into organised co-operative concerns, and their problem now was how to meet their deficits. "The method of setting wards aside for paying patients might vitally affect the very essence of the voluntary hospital and turn it into a quasi-commercial nursing home. The only solution now is the way which adds State charity to the resources and achievements of private charity. When the community gives, as well as private persons, it makes a fairer and more equitable world." In answer to the question how aid should be given by the State, Professor Barker put forward the analogy of university. The University Grants Committee receives an annual Parliamentary grant of some £2,000,000 and distributes this among the universities,

attaching no specific conditions. "A Hospital Grants Committee might receive an annual Parliamentary grant; and probably a system of regional hospital councils, acting on behalf of the committee in the same way as the central federal authority of the University of London acts on behalf of the University Grants Committee, might be a further necessity." He claimed that this idea was in tune with the General English way of doing things. So far from defeating self-help or drying up the springs of private charity, it was likely to stimulate and increase them. "The grants made by the State to universities, have not diminished the private support and the private endowment of universities. The plan is an economic one, and a good and valid alternative to the other and far more costly method to which we might otherwise be driven the method by which the State, owing to the failure of unassisted voluntary effort to face the gigantic task of maintaining voluntary hospitals, would be forced to take them over and to run them at a far greater cost."

## Notice—Dental Diploma

### COLLEGE OF PHYSICIANS AND SURGEONS OF BOMBAY.

**Regulations relating to the Examinations for Licence  
in Dental Surgery.**

#### (ABSTRACT).

#### SECTION I.

A candidate for the Licence in Dental Surgery of the College of Physicians and Surgeons of Bombay shall pass three professional examinations, hereinafter called the First Examination, the Second Examination and the Final Examination.

The curriculum of professional study extends over a period of four years subsequent to admission in a recognised Dental School after passing the Intermediate Examination in Science of the University of Bombay in the group of Chemistry, Physics and Biology or an examination recognised by the College as equivalent to it.

Candidate may take the whole or part of the examination. The fees payable for these examination shall be:—

|                                |                                                  |
|--------------------------------|--------------------------------------------------|
| For the First Examination ...  | { Part I Rs. 40<br>Part II „ 20<br>Part III „ 20 |
| For the Second Examination ... | „ 20                                             |
| For the Final Examination ...  | { Part I „ 30<br>Part II „ 50                    |

A candidate must apply, through the Head of his Dental

School, for permission to appear at any of the examinations, at least three weeks before the date of commencement of the examination.

The fee for the examination is payable seven days before the date of the commencement of the examination, and should not be forwarded with the application form. The fee once paid shall not be refunded or reserved for any future examination.

To pass the examination a candidate must obtain in each subject 40 per cent of the full marks in the written test, 40 per cent in each of the oral, clinical and practical tests and 50 per cent in the written, oral, clinical and practical tests taken together.

Any candidate who fails to pass or to present himself at any examination may be re-admitted to one or more subsequent examinations, subject to the following conditions:—

(a) That a fresh application is made and a fresh fee is paid.

(b) That certificates are submitted to show that the candi-

#### Notice—Dental Diploma

date has, during the interval since last appearing at the examination pursued a further course of studies in the subjects of the examination for a period of at least one full session to the satisfaction of the Head of his School.

The courses of Medicine, General Pathology and Surgery for dental students must be conducted by Physicians and Surgeons who are in the habit of teaching medical students, but in classes separate from those of the medical students.

Candidates appearing for the examination or part of the examination will have to produce a certificate of good moral character and of diligent study.

#### SECTION II.

##### THE FIRST EXAMINATION.

1. The subjects for the First Examination are:—

Part I—Dental Mechanics and Dental Metallurgy.

Part II—General Anatomy and Physiology.

Part III—Special Anatomy and Physiology of the teeth and associated parts.

#### SECTION III.

##### THE SECOND EXAMINATION.

1. The subjects of the Second Examination are:—

Medicine, General Pathology and Bacteriology.

#### SECTION IV.

##### THE FINAL EXAMINATION.

1. The subjects for the Final Examination are:—

Part I—General Surgery (including Surgical Pathology).

Part II—Dental Surgery and Pathology, and Practical Dental Surgery.

Candidates appearing for the Final Examination in Dentistry will be required to produce satisfactory evidence of having attained the age of 21 years.

#### Special Regulations relating to Exemptions.

Exemption from Part II of the First Examination will be granted to a candidate who has passed the First L.C.P.S. or the Intermediate M.C.P.S. Examination of this College or the First M.B., B.S. Examination of the University of Bombay, or who has obtained exemptions in the subjects of Anatomy and Physiology at the First L.C.P.S. Examination. A candidate so exempted can complete the Dental Diploma course in three years after joining a recognised Dental and Medical School and Hospital. In his case rule 3 of section IV will be waived. No study for the subjects of Part II of the Final Examination will be recognised until the candidate has passed Part III of the First Examination. Also he must pass the whole of the First Examination before being allowed to appear at Part II of the Final Examination.

A candidate who produces satisfactory evidence from the Head of an affiliated Medical School or College of having kept the requisite terms for either the First L.C.P.S. or the Intermediate M.C.P.S. Examination of this College or the First M.B., B.S. Examination of the University of Bombay will be allowed to enter for Part II of the First Examination, after passing which he can complete the Dental Course in three years.

Exemptions from Part II of the First Examination, from whole of the Second Examination

and from Part I of the Final Examination will be granted to a candidate who has passed the Final L.C.P.S. or M.C.P.S. Examination of this College or the Final M.B., B.S. Examination of the University of Bombay or who has obtained exemptions in the subjects of Medicine and Surgery at any of these examinations. A candidate so exempted can complete the Dental Diploma course in two years after joining a recognised Dental School and Hospital; but he must pass in Parts I and III of the First Examination before being allowed to take Part II of the Final Examination.

## Service News and Notes.

**1. Private Practice by Government Medical Officers.**—Recently members of the service have been considerably perturbed over the proposals by Government to curtail their right of private practice. Members have already been informed of the steps taken by the Executive Committee to protect as far as possible the existing interests of existing officers. An extraordinary meeting of the General Body was held on the 1st November 1938 to consider this question. At that meeting the Executive was authorised to explore all possible avenues of redress. The Executive is now 'seized of the matter' once again. Members have been informed separately again of what has been done in the matter.

**2. Annual General Meeting.**—The next Annual General Meeting is due to be held about the end of December 1938. In view of the general appreciation of the **Subscription Dinner** arranged last year on the day of the Annual General Meeting, the Executive Committee has proposed to keep up the idea of the social gathering before the business meeting. The time and place of the Dinner and the Meeting will be communicated to members in due course. In the meantime such of the members as are willing to meet their brethren in service will send their subscription of Rs. 2-8-0 towards the cost of the dinner to the

Treasurer, Dr. S. Ramakrishnan, Department of Bacteriology, Medical College, Madras.

**3. Retirements.**—Since the issue of the last number of the Journal, three members of the service have gone on leave preparatory to retirement. Dr. Miss P. Samuel and Dr. C. Ramamurti are retiring on superannuation early next year. We wish them well of their retired life. We hope they will not lose their interest in the affairs of the Association.

Dr. S. K. Pillai, the late Personal Assistant to the Surgeon-General, retires much ahead of his superannuation age. He has deserved very well of the Association though individuals may have personal grievances and no Personal Assistant can possibly satisfy everybody. Dr. Pillai has always had the interests of the service in his heart. He has silently contributed his mite towards the welfare of the service. He is keen on doing some social service on retirement. We hope that Madras will not lose his service even though his official career has ceased.

In response to a proposal from the Executive Committee there was a widespread response from members of the Association to do honour to the retiring Personal Assistant. An informal Tea was given to Dr. Pillai on the 1st Nov-

ember 1938, at which nearly 70 members were present including a few from the mofussil.

**4. Obituary.**—We very much regret to record the death of Major A. Krishnamurti. Our hearty condolences are due to the bereaved family.

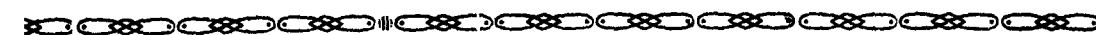
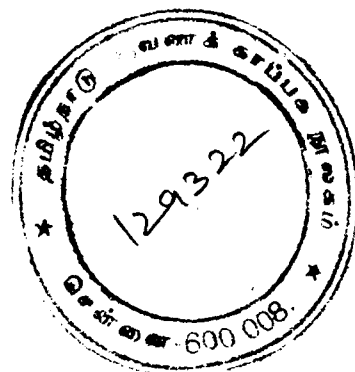
**5. Felicitations.**—One of the most momentous events in the annals of the Service is, however, the recent appointment by Government of our President, Dr. A. Lakshmanaswami Mudaliar, as Principal of the Madras Medical College, Madras, in the vacancy caused by the going on leave preparatory to retirement of Lt.-Col. Plumptre. The Association has cause to be proud that, *even in its decadence*, the claims of the Provincial Medical Service have been recognised by Government in filling the post of the head of a premier medical institution in India. Of the unique personal qualifications of Dr. Mudaliar it is unnecessary for us to say anything.

We offer our felicitations to the new Personal Assistant,

Major T. V. Rajaratnam. His is a thankless, onerous task, especially now that the service has no friends. We are sure that consistent with the responsibilities attaching to his Office, he will have the interests of his service, and its existing incumbents at the back of his mind.

We congratulate Dr. G. Dinker Rau, on his appointment as Additional Professor of Medicine Madras Medical College, Madras, an appointment until recently permanently held by I. M. S. officers.

**6. Ourselves.**—We fear that this will be the last number of the *Madras Medical Journal*. As we have had repeatedly bewailed, members of the Association have shown absolutely no interest whatever in the Journal. We are therefore recommending to the Executive Committee to give up the idea of publishing the Journal unless somebody else is willing to take up the burden of conducting the Journal against all possible odds that we have had to fight.



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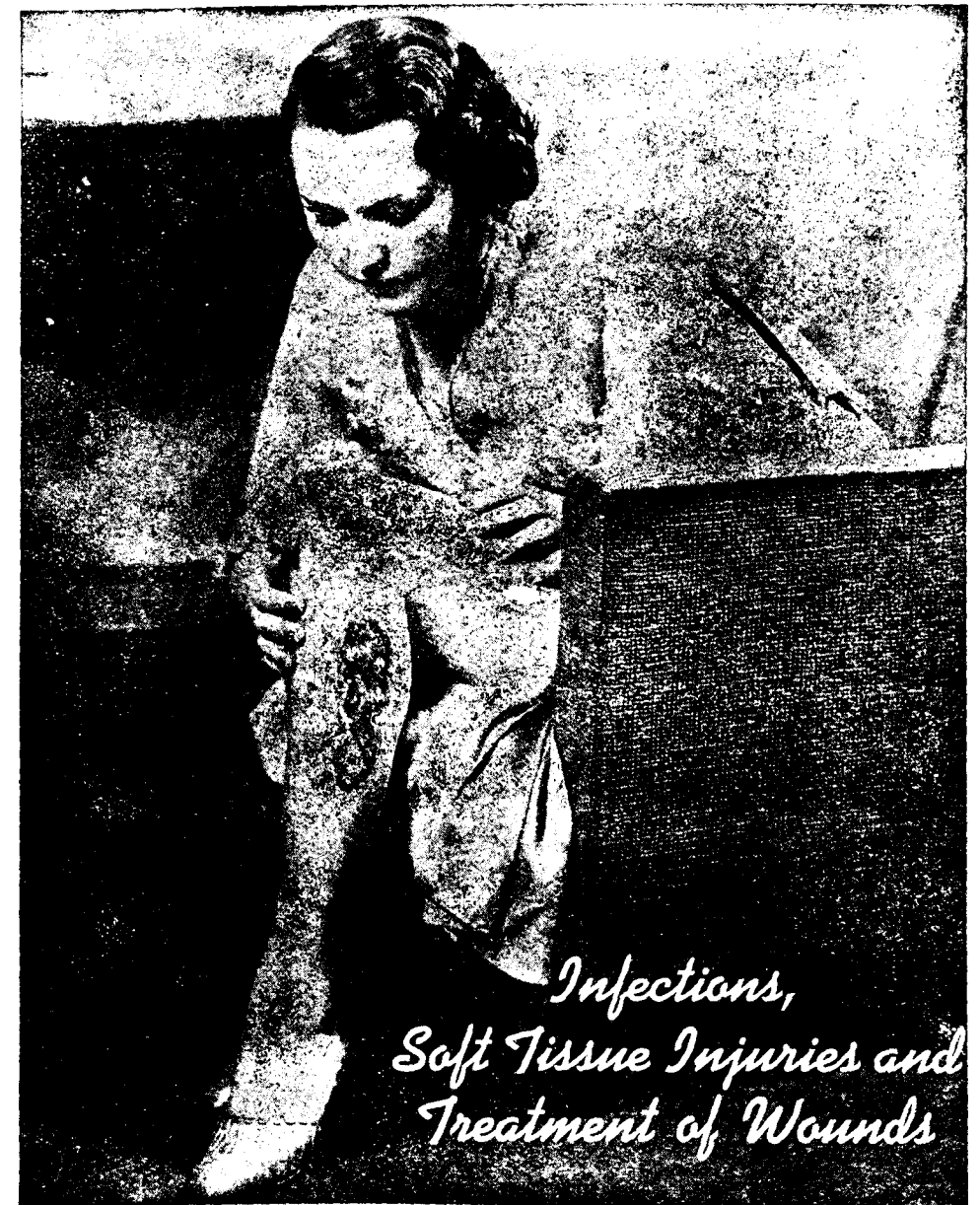
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