an injection of one of the other vaccines it is desirable to allow at least three weeks to elapse.

(*i*) B.C.G. vaccine may be given to schoolchildren aged 10 years or more at the discretion of the Medical Officer of Health. (Circular 6/61.)

SCHEDULE Q

| Age | Visit | Vaccine | Injection | Interval |
|---|---|---|---|---|
| 6 to 8 months | 1 | Poliomyelitis 1 | 1 | 4 weeks |
| | 2 | „ 2 | 2 | |
| 9 to 12 months | 3 | Diphtheria, pertussis, tetanus 1 | 3 | 4–6 weeks |
| | 4 | Diphtheria, pertussis, tetanus 2 | 4 | |
| 15 to 18 months | 5 | Poliomyelitis 3 | 5 | |
| 18 „ 21 „ | 6 | Diphtheria, pertussis, tetanus 3 | 6 | |
| Smallpox during the first 2 years but preferably at 4–5 months (see Note *f*) | | | | |
| School entry ... | | Poliomyelitis 4, diphtheria, and tetanus | | |
| 8 to 12 years ... | | Diphtheria and tetanus. Smallpox revaccination | | |
| Over 12 „ ... | | B.C.G. (see Note *g*) | | |

NOTES

(*a*) On this schedule, no antigen is given *by injection* before the age of 6 months, which increases the possibility of a maximal antibody response.

(*b*) Two doses of poliomyelitis vaccine are given before any other injection, and, although it cannot be accepted as proved, this might well reduce the risk of "provocation" paralysis which would otherwise be increased owing to the use of the combination of pertussis vaccine with toxoids.

(*c*) Vaccination against pertussis is delayed until between 9 and 12 months; thus no direct protection is offered against the risk of death among younger infants. On the other hand, the time of vaccination in this schedule is nearer to the time of maximum incidence of the disease, and this may indirectly protect infants by reducing their chances of being infected by older children.

(*d*) The number of visits and injections is smaller than in Schedule P, but it is possible that if immunization is postponed until the baby is six months old it may be less easy to gain the continued co-operation of the parents. Early vaccination against smallpox would, however, help to keep the mother in touch with the doctor.

(*e*) Should it be desired, visit 6 may be avoided by giving poliomyelitis 3 and diphtheria/pertussis/tetanus 3 at different inoculation sites during visit 5.

(*f*) An interval of at least two weeks should normally be allowed to elapse after an injection of diphtheria/pertussis/tetanus or poliomyelitis vaccine before undertaking vaccination against smallpox. When vaccination against smallpox precedes an injection of one of the other vaccines it is desirable to allow at least three weeks to elapse.

(*g*) B.C.G. vaccine may be given to children aged 10 years or more at the discretion of the Medical Officer of Health. (Circular 6/61.)

# NOMENCLATURE OF HAEMOGLOBINS

*The following recommendations on the nomenclature of haemoglobins have been sent to us by Professor V. M. Ingram, of the Department of Biology of the Massachusetts Institute of Technology, and Dr. P. S. Gerald, of the Children's Hospital Medical Center and Harvard Medical School, Boston. The proposals originated during a "Haemoglobin Structure Workshop" held in Boston in December, 1960. The recommendations are also appearing in the August issue of the "Journal of Biological Chemistry."*

## Chain Nomenclature

There is now general agreement on the naming of the peptide chains of the major components of normal human adult and foetal haemoglobins as the $\alpha$, $\beta$, and $\gamma$ chains—e.g., adult haemoglobin is written as $\alpha_2^A\beta_2^A$ and foetal haemoglobin as $\alpha_2^A\gamma_2^F$. The superscripts A and F refer to the fact that the particular chain is the one found in the human adult and foetal haemoglobins. It is recommended that this practice be continued and that the symbols $\alpha$, $\beta$, and $\gamma$, without superscripts, be reserved for those occasions when reference is being made to, for example, chains in general.

Information concerning the structure of the chains of haemoglobin $A_2$ is now sufficient to indicate that one of the chains is identical with the $\alpha^A$ chain, while the second differs in a number of residues from the three foregoing chains. In addition there is evidence (e.g., Cepellini[1]) to indicate that the genetic control of this unique chain is independent of the genes for the $\alpha$, $\beta$, and $\gamma$ chains. It is therefore recommended that this chain be designated as $\delta^{A_2}$; Hb $A_2$ is then written as $\alpha_2^A\delta_2^{A_2}$. Again, one could refer simply to $\delta$ chains in the general case.

The simplest method of naming the tryptic peptides of a chain is to number them in the order in which they occur in the chain, beginning with the N-terminus. The symbol for the chain is included as a part of the designation. The letters Tp are included to identify that these are the peptides obtainable by tryptic digestion. For example, the third tryptic peptide of the $\alpha$ chain would be $\alpha$TpIII in this system. Where a lysyl bond is not attacked under the conditions used, the symbol for the resultant "dipeptide" or "double peptide" would contain the numbers appropriate to both tryptic peptides—e.g., $\alpha$TpI,II. From the published structure of the $\alpha$ and $\beta$ chains[2–4] and from the amino-acid composition, it is evident that the $\alpha$ chain will contain the tryptic peptides $\alpha$TpI to $\alpha$TpXIV and the $\beta$ chain the tryptic peptides $\beta$TpI to $\beta$TpXV. It so happens that the tryptic "peptides" $\alpha$TpVIII and $\beta$TpVIII are lysine. In addition, the present methods of tryptic cleavage do not break the bond separating the expected tryptic peptides $\alpha$TpXII and $\alpha$TpXIII, nor the bond between the expected peptides $\beta$TpX and $\beta$TpXI. In view of the possibility that these bonds might be split in some experiments at a later date, it is felt that the numbering system should correspond with the theoretical number of tryptic peptides. When the complete sequence of the chains is determined beyond question and is published, then a more specific designation involving residue numbers should be adopted. Thus, $\beta$TpI can be designated as $\beta$Tp1–8.

## Nomenclature of Abnormal Haemoglobins

An ideal nomenclature system for the abnormal haemoglobins would provide for adequate designation of the chemical structure at each stage of the investigation. The following system is an attempt to meet this requirement.

When only the chain in which the abnormality resides is known, then the haemoglobin may be written as $\alpha_2^A\beta_2^S$, or $\alpha_2^A\beta_2^{D\text{Punjab}}$. When the abnormality has been located in a particular tryptic peptide, as by fingerprinting, then the designation should be, for example, $\alpha_2^A\beta_2^{\text{TpI}}$. When the amino-acid composition of the tryptic peptide indicates a particular amino-acid substitution, then this will be indicated as $\alpha_2^A\beta_2^{\text{TpI(Glu}\rightarrow\text{Val)}}$ for Hb S. Finally, when the amino-acid interchange has been located at a particular residue position in the chain, the fully descriptive formula, as in the case of Hb S, would be in the form : $\alpha_2^A\beta_2^{6\text{Val}}$.

Presumably, for use in formulae describing experiments such as reassociation, it will be necessary to define in a given paper a one-letter designation for a particular haemoglobin. For example, the formula $\alpha_2^I\beta_2^S$ could be used, provided that wherever possible the individual haemoglobins have been defined, as, for example, Hb I as $\alpha_2^{16\text{Asp}}\beta_2^A$ and Hb S as $\alpha_2^A\beta_2^{6\text{Val}}$. It is strongly urged that no further letters be assigned to abnormal haemoglobins. Newly discovered haemoglobins, prior to their chemical identification, should be known by the letter designation of the previously described haemoglobin whose electrophoretic mobility they most nearly resemble. To the letter should be attached a subscript indicating the geographic origin of the new haemoglobin.

(*Continued at foot of page 765*)

# To-day's Drugs

*With the help of expert contributors we publish below notes on a selection of drugs in common use.*

**Meprobamate**

"Equanil" (Wyeth).
"Mepavlon" (Imperial Chemical (Pharmaceuticals)).
"Miltown" (Wallace).

*Chemistry.*—This is 2-methyl-2-n-propyl-1:3-propanediol dicarbamate.

*Pharmacology.*—Although chemically related to the muscle-relaxant drug mephenesin, mebrobamate has little effect as an internuncial depressant. It produces sedation, with general slowing of the electroencephalograph, and has an effect on the higher parts of the central nervous system at least as much as on the lower. Most of the experimental work has compared meprobamate with chlorpromazine and other newer tranquillizers. Comparisons with barbiturates have not been properly carried out, but it is known that meprobamate and barbiturates are synergistic. The drug is comparatively non-toxic.

*Therapy.*—Meprobamate is said to be a mild tranquillizer, a class of drug that is considered in itself to have less hypnotic effect than, say, barbiturates, so it is perhaps hardly surprising that the drug has little therapeutic effect. In some tense patients it is undoubtedly effective as a mild sedative, but, in spite of being chemically related to the muscle-relaxant mephenesin, it is of no special value in treating those patients with prominent muscular tension and secondary "rheumaticky" pains—e.g., at the back of the neck. Clinical studies make it doubtful if it is better than phenobarbitone for psychiatric disturbances; it is of less value for the more seriously disturbed patients, including psychotics. In neurological diseases entailing spasticity of muscles, meprobamate sometimes decreases the muscle spasm, and even patients with Parkinsonism may be benefited.

Meprobamate has perhaps a small place as one of the group of drugs producing mild sedation, ringing the changes on which will enable some chronically tense patients to be kept going. It has no specific advantages over any other such drug, nor is there any unique indication for its use. The drug acts synergistically with other sedatives, including barbiturates, but combined treatment gives a false impression of getting the same sedation with less "drugging," since meprobamate is not freer than barbiturates from undesirable depressant effects.

*Toxic Effects.*—A wide variety of toxic effects have been reported, but most of them are rare. Skin rashes of all sorts are the commonest, and general hypersensitivity reactions next. Habituation, and even addiction, can occur, but very rarely. After heavy and prolonged administration, abrupt withdrawal will produce a syndrome of tremulousness, gastrointestinal disturbances, and sometimes convulsions. Suicide can be successfully committed with meprobamate.

*N.H.S. Basic Price.*—400-mg. tabs., 100 for 15s. 5½d.

(*Continued from page 764*)

Proposals similar to the above originated during the Haemoglobin Structure Workshop held in Boston, December 14–16, 1960. These proposals have been modified at the suggestion of other workers in the protein-structure field. In their present form they represent a compromise between the views of these two groups.

REFERENCES

1 Cepellini, R., Contribution to Ciba Symposium on Biochemical Genetics, 1959.
2 Braunitzer, G., Rudloff, V., Hilske, K., Liebold, B., and Mueller, R., *Hoppe-Seylers Z. physiol. Chem.*, 1960, **320**, 283.
3 —— ibid., 1960, **322**, 96.
4 Hill, R., and Konigsberg, W., *J. biol. Chem.*, 1961, **236**, PC7.

# Correspondence

*Because of heavy pressure on our space, correspondents are asked to keep their letters short.*

## Seasonal Incidence in Clinical Onset of Hodgkin's Disease

SIR,—We have been much interested in the report from the Royal Marsden Hospital by Dr. Marion D. Cridland (September 2, p. 621) suggesting a seasonal incidence in the clinical onset of cases of localized Hodgkin's disease, many of which appear to arise in the month of December. As Dr. Cridland indicates that comparable studies might be made elsewhere and as we are at present reviewing a series of 440 histologically proven cases seen at the department of radiotherapy at Edinburgh Royal Infirmary since 1936, we have abstracted the relevant figures from this group.

We have followed exactly the criteria adopted by Dr. Cridland for the selection and exclusion of cases, so that the results should be as closely comparable as possible. In the Royal Marsden series of 269 cases 106 were accepted as true localized cases, whereas in the Edinburgh series a much smaller proportion, 104 out of 400 cases, could be similarly classified. In these the ratio of males to females was 2:1, the same as in the London group. The Table below has been drawn up in the same manner as Dr. Cridland's results were presented to show the seasonal onset of cases in the Edinburgh and London series and in the combined series of 210 cases.

| Month of Onset | Edinburgh (104 Cases) | | London (106 Cases) | | Combined Series (210 Cases) | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| January | 19 | 18·2 | 14 | 13·2 | 33 | 15·7 |
| February | 11 | 10·6 | 6 | 5·7 | 17 | 8·1 |
| March | 13 | 12·5 | 4 | 3·8 | 17 | 8·1 |
| April | 4 | 3·8 | 9 | 8·5 | 13 | 6·2 |
| May | 1 | 0·9 | 7 | 6·6 | 8 | 3·8 |
| June | 9 | 8·6 | 7 | 6·6 | 16 | 7·6 |
| July | 13 | 12·5 | 4 | 3·8 | 17 | 8·1 |
| August | 6 | 5·8 | 6 | 5·7 | 12 | 5·7 |
| September | 2 | 1·9 | 12 | 11·2 | 14 | 6·6 |
| October | 15 | 14·4 | 5 | 4·7 | 20 | 9·5 |
| November | 5 | 4·8 | 9 | 8·5 | 14 | 6·6 |
| December | 6 | 5·8 | 23 | 21·7 | 29 | 13·8 |

It will be seen that, while the Edinburgh figures show a more random distribution of seasonal incidence, 41.3% of the cases occurred between January and March, and in the combined series December and January are undoubtedly the months of maximum incidence.

Having made this study to compare with Dr. Cridland's findings we feel hesitant to draw conclusions regarding a possible causal infective agent in the disease. It must be realized that the results are entirely dependent on the ability of patients to recall the month in which they first noticed enlarged lymph nodes. Unless the nodes had enlarged rapidly there is no way of being certain that the onset of the disease occurred in this month, and furthermore it is a not uncommon experience to discover quite large superficial nodes of which the patient is unaware.

As the cause of Hodgkin's disease and other reticuloses remains unknown it would seem that the need continues for all studies that may throw further light on the natural history of these disorders.—We are, etc.,

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