

history, and to contain more complicated cases, than those admitted on other days. Evidently people are unwilling to disturb their doctor on Sundays, and if they have appendicitis this may have unfortunate results. R. H. Jackson<sup>3</sup> has also emphasized that many parents still do not appreciate the seriousness of certain abdominal symptoms in children, while at the other end of life Wallace and his colleagues found that none of their patients over the age of 65 had histories of less than 12 hours, and most had complications.

Wallace and his co-workers also showed the perennial risk run by young women of having a normal appendix removed. Recent studies by H. E. Harding<sup>4</sup> and J. A. H. Lee<sup>5</sup> have confirmed the size of this problem, and also the rather close age limits. The excess predisposition to this mishap begins at the age of 14, is at a maximum at 17, and has disappeared (both in the married and the single) by 24. Probably this situation will continue until the gynaecological condition which mimics appendicitis so closely in these girls is described and its differentiation from appendicitis is clarified. At least it would help to have a diagnostic label to apply to these cases where the pathologist fails to find any evidence of inflammation of the appendix.

## The "Pill" and Thrombosis

One of the first instances of thrombophlebitis in a woman taking oral contraceptives was recorded in Great Britain in 1961.<sup>1</sup> This week in a letter at p. 1132 Dr. K. J. Zilkha reports the occurrence of cerebrovascular incidents in two young women taking oral contraceptives. In 1962 an international meeting was convened to study the problem and 118 cases were reported, including some deaths.<sup>2</sup> Whether the contraceptive pill was the cause of this mortality and morbidity in otherwise healthy women was not clear, but the debate emphasized our ignorance of the incidence of thrombophlebitis in normal women of child-bearing years.

Statistics from Canada and North America suggested that there were three cases of thrombophlebitis per 1,000 per year, but the information was obtained from retrospective surveys, and S. Sevitt and N. G. Gallagher<sup>3</sup> have shown how unreliable the clinical assessment of venous thrombosis may be. So far there is no firm evidence to indicate that the incidence in patients on oral contraceptives exceeds this figure. Any misgivings could be resolved only by a prospective study of thromboembolism in normal women and, concurrently, women on the "pill."

Laboratory studies have also not yet been conclusive in deciding whether oral contraceptives produce an increased clotting tendency.<sup>4</sup> Both during normal pregnancy and in the puerperium women often develop thrombophlebitis, and there is a rise in the concentration of several of the coagula-

tion factors of the blood.<sup>5-7</sup> Oral contraceptive hormones simulate pregnancy and may raise the concentration of clotting factors. Thus O. Egeberg and P. A. Owren<sup>8</sup> found increased levels of factor VIII (anti-haemophilic globulin) and factor VII in five women who were taking norethynodrel (Enavid). Both these factors are known to be increased in pregnancy and a rise in factor VII has also been found in patients who have had a recent thrombosis.<sup>9</sup> The importance of the rise in the level of factor VIII is not clear, as this change has not been found in thrombosis, and in fact thrombosis has occurred in a patient suffering from haemophilia—in which, of course, factor VIII is congenitally deficient.<sup>10</sup> In contrast, L. Poller and J. M. Thomson<sup>11</sup> found that a rise in factor VIII occurs also in patients who are treated on a long-term basis with coumarin anticoagulants. The information so far available suggests that a slight increase in coagulation factors occurs in some women taking oral contraceptives, but the importance of the changes is uncertain. Recently workers in the United States<sup>12</sup> have reported an increase in the number of spontaneous thrombi formed in the hearts of hamsters receiving norethynodrel, though the dose given was comparatively enormous.

After considerable propaganda and favourable reports in the popular press the number of women taking the "pill" has recently increased considerably in Britain and may amount to nearly a quarter of a million. The publicity has usually been coupled with a warning about previous thrombophlebitis, but the fear of causing unnecessary thromboembolism in healthy women will no doubt still deter many doctors from prescribing oral contraceptives widely. It is in the interests of all concerned—the general public, the family planners, and the drug companies—that the many preparations now available should be shown to be safe. Studies at present in progress in Britain and elsewhere may help to do this.

## Intracranial Haemorrhage in Haemophilia

According to C. B. Kerr<sup>1</sup> intracranial haemorrhage is now the most common cause of death in haemophiliacs, and it has not been influenced by modern therapy to the same extent as has post-operative or traumatic bleeding at other sites. He studied 109 haemophiliacs (including 17 with Christmas disease) over a period of five years, when fifteen of them suffered nineteen episodes of proved or probable intracranial haemorrhage, the mortality being 33%. In only five of these nineteen episodes was trauma certainly the cause, and only once was this severe enough to make the patient lose consciousness. Moreover, on inquiry it was discovered that 13 of the 109 patients had previously experienced "major" head injuries without complication, and that four of these were boxers who had between them performed in 144 bouts without incident, even though they had been in hospital as a result of their disease on a total of 50 occasions.

The risks of needling and of incision have often precluded modern neuroradiological methods of investigation, so that

<sup>1</sup> Jordan, W. M., *Lancet*, 1961, 2, 1146.

<sup>2</sup> *Thromboembolic Phenomena in Women*. Proceedings of a conference, 1962. Searle, Illinois.

<sup>3</sup> Sevitt, S., and Gallagher, N. G., *Lancet*, 1959, 2, 981.

<sup>4</sup> *Brit. med. J.*, 1963, 1, 207.

<sup>5</sup> Koller, F., Loeliger, H., and Duckert, F., *Rev. Hémat.*, 1952, 7, 156.

<sup>6</sup> Alexander, B., Meyers, L., Goldstein, R., Gurevitch, V., and Grinspoon, L., *J. clin. Invest.*, 1954, 33, 914.

<sup>7</sup> Preston, A. E., *Brit. J. Haemat.*, 1964, 10, 115.

<sup>8</sup> Egeberg, O., and Owren, P. A., *Brit. med. J.*, 1963, 1, 220.

<sup>9</sup> Poller, L., *J. clin. Path.*, 1957, 10, 348.

<sup>10</sup> Borchgrevink, C. F., *Lancet*, 1959, 1, 1229.

<sup>11</sup> Poller, L., and Thomson, J. M., *ibid.*, 1964, 2, 62.

<sup>12</sup> *Medical Tribune*, 4 May 1964, p. 1.

<sup>1</sup> Kerr, C. B., *J. Neurol. Neurosurg. Psychiat.*, 1964, 27, 166.

<sup>2</sup> Silverstein, A., *Arch. Neurol. (Chic.)*, 1960, 3, 141.

<sup>3</sup> Simpson, D. A., and Robson, H. N., *Aust. N.Z. J. Surg.*, 1960, 29, 287.

<sup>4</sup> Marfarlane, R. G., *et al.*, *Lancet*, 1957, 2, 251.