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Schizophrenia and related psychoses CHAPTER 1 Venous thromboembolism Evidence of an association Antipsychotic treatment was first linked to an increased risk of thromboembolism in 1965.1 Over a 10-year observation period, 3.1% of 1,590 patients developed thromboembolism, of whom 9 (0.6%) died. However, the use of antipsychotic medication is a proxy for severe and enduring mental illness and so observed associations with anti psychotics may at least partly reflect inherent pathological processes in the conditions for which they are prescribed. To some extent, the relative contributions to the risk of thromboembolism of antipsychotic treatment and the conditions they treat remain to be clearly defined. In a case–control study of nearly 30,000 patients,2 risk of thromboembolism was greatly increased overall in people prescribed antipsychotics (odds ratio [OR] 7.1). The increased risk was driven by low-potency phenothiazines (thioridazine, chlorpromazine; OR 24.1) and was seen chiefly in the first few weeks of treatment. Absolute risk of VTE was low – it was seen in only 0.14% of patients (about 1 in every 714 people). A secondary analysis suggested no association with diagnosis, apparently ruling out an association with schizophrenia itself. A later meta-analysis of seven case–control studies3 confirmed an increased risk of thromboembolism with low-potency FGAs (OR 2.91) and suggested lower but significantly increased risks with all types of antipsychotics. Later, a meta-analysis of 17 studies4 reported a small increased risk of thromboembolism with antipsychotics as a whole (OR 1.54) and with FGAs (OR 1.74) and SGAs (OR 2.07) as individual groups. Risk of thromboembolism clearly decreased with age. The authors suggested that the best that could be said was that antipsychotics probably increased the risk by about 50% but that residual confounding could not be discounted (i.e. other factors may have accounted for the effect seen). Since this time, several more case–control studies have confirmed both the slightly increased risk of thromboembolism and the small risk overall.5–7 One study reported a risk for older people taking antipsychotics as 43 per 10,000 patient years.7 Other noteworthy findings were a substantially increased association with thromboembolism for prochlorperazine – a drug not always (or even often) prescribed for psychotic disorders5 – and an increased risk linked to antipsychotic dosage (risk was quadrupled in high-dose patients).6 An association with prochlorperazine prescribing had previously been suggested by a UK study.8 These findings add weight to the theory that antipsychotic medication (and not only the conditions it treats) is responsible for the increased hazard of thromboembolism. The highest risk of pathological blood clotting may be in the first 3 months or so of treatment.9,10 Several meta--analyses have been published in recent years. The findings of two studies are presented in Table 1.49.

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