young children when the heart rate is slow and the child is lying on its side. Thayer believes this is due to the increased tension in the mitral valve caused by the sudden inrush of blood at the beginning of diastole.

The first and second sounds are composite, each, according to Sprague and Rappaport, comprising four separate entities. The first is due to vibrations set up by auricular systole, the isometric contraction phase of the ventricles, the opening of the semilunar valves, and the acceleration of blood in the great vessels during the maximum ejection phase of ventricular systole. The second sound is due to ventricular vibration during relaxation at the beginning of diastole, the closure of the semilunar valves, the vibration of the blood column and walls of the great vessels, and the opening of the mitral and tricuspid valves. Any deviation from the normal in the time relationship of the conduction of impulse, or contraction of muscle, or disturbances in pressure relationship in the pulmonary or aortic systems may cause separate components of one or both sounds to be recognizable as individual entities. This may lead to a split or, if definitely separate, a reduplicated heart sound, or even a completely separate third or fourth heart sound. A deep breath may occasion this in a normal individual by increasing the pressure gradient between aorta and left ventricle and diminishing it between right ventricle and pulmonary artery. A prolonged PR interval in latent heart-block may allow the auricular contraction to be heard separately from the ventricular sounds, or in bundle-branch block asynchrony of contraction of the ventricles may cause a reduplicated first sound or first and second sounds.

A gallop rhythm usually refers to an easily recognizable third heart sound in diastole when the heart rate is over 100 per minute and there are obvious signs of cardiovascular disease. It may be a protodiastolic or presystolic gallop rhythm, according to whether the third heart sound occurs in mid- or late diastole. Dock has shown that both are due to sudden tensing of the valves from rebound of the ventricle following the unusually rapid inflow which occurs when the auricular pressure is elevated. It is a sign of ventricular dilatation and impending or actual congestive failure. These added sounds can be differentiated clinically only by assessing the case as a whole and after full examination, including screening of the patient.

Chronic Cold Feet

Q.—*A man aged 53 has had increasingly cold feet for the past ten years. He has suffered a good deal of pain during the past three winters and now has a tender black spot the size of a pin-head on each great toe. B.P. 150/90; pulsation in post-tibial and dorsalis pedis arteries; his general health is good and his hands are normal. Is any drug treatment worth trying? Could nicotinic acid or nicotinamide help?*

A.—The description suggests that this patient has the distal type of peripheral vascular disease in which the occlusive process is chiefly in the small vessels of the foot. The effects of treatment in such patients are often disappointing. The all-important point in management is the inculcation of the most rigid hygienic discipline in the care of the feet. Vasodilator drugs should certainly be employed: nicotinic acid (not nicotinamide) appears to help some, and carbachol has occasionally been successful. It would be advisable to seek the opinion of a surgeon on the desirability of lumbar ganglionectomy.

Lupus Vulgaris and Pregnancy

Q.—*I have a patient with lupus vulgaris who has been ordered by a dermatologist to take 50,000 units of calciferol twice daily. She has now become pregnant. Is calciferol in such doses contraindicated? Is the pregnancy likely to affect the lupus vulgaris?*

A.—Pregnancy does not often have a significant effect on lupus vulgaris. In some cases the condition appears to be activated slightly but not to the extent of causing any serious anxiety. Nor does pregnancy contraindicate treatment with calciferol in the dose mentioned. However, the patient needs to be kept under close observation during treatment, and regular and frequent testing of the urine and blood pressure is important. Treatment should be suspended in the presence of either albuminuria or hypertension, or if the patient develops any toxic symptoms attributable to the calciferol. Here there may be some difficulty, for common toxic symptoms such as anorexia, nausea, vomiting, and lassitude might be confused with similar symptoms associated with the pregnancy itself. Estimation of the serum calcium level might be carried out from time to time as an additional precaution.

Benadryl and Agranulocytosis

Q.—*Is agranulocytosis or any other dangerous blood condition likely to develop from the administration of 50 mg. of "benadryl," three times a day for a period of six to eight weeks?*

A.—Benadryl has been used very widely since its introduction in 1946, and there has been plenty of opportunity to observe the occurrence of agranulocytosis if that was produced by taking benadryl. So far there has been no record of this, and it may safely be concluded that there is no risk of "a dangerous blood condition" arising from the proposed treatment.

Stability of Calcium Chloride and Ammonium Bromide

Q.—*Are calcium chloride and ammonium bromide stable in solution? I mean a solution kept as stock for dispensing. Could you give me the approximate solubility of calcium chloride?*

A.—Both calcium chloride and ammonium bromide are perfectly stable in aqueous solution, and the usual strength for a stock solution for dispensing is 1 in 6. Calcium chloride is very deliquescent and is soluble to the extent of about one part in one and a half parts of water. Ammonium bromide has approximately the same solubility.

Pasta Picis Carbonis

Q.—*Tar being a carcinogenic substance, is it unwise to use pasta picis carbonis (B.P.C.) for other than brief periods? If so, what would be considered a safe period of time?*

A.—The carcinogenic potency of liquor picis carbonis has recently been tested by Berenblum, whose report on this subject appears elsewhere in this issue (p. 601). His earlier work was discussed in the twenty-fifth annual report of the British Empire Cancer Campaign (1947, p. 133). Spectrographic analysis showed its benzpyrene content to be about 0.02%. Biological tests, consisting of twice-weekly painting of mouse skin, yielded seven tumours in 12 mice treated; of these tumours, four subsequently became malignant. While this result is properly regarded as having clinical interest, the risk of tumour induction following application of the liquor or paste in man is probably very small. It is, however, impossible to indicate any safe period, and it would be advisable for their application, especially for lengthy periods, to be subject to regular medical supervision; meantime, as Berenblum says, "avoidance of *long-continued* application of liquor picis carbonis would be a wise precaution." Berenblum's article and the general problem raised by this question are further discussed in an annotation at p. 608 of this issue.

Correction

In the issue of Sept. 4 (p. 489) it was stated that a short full-time intensive course in paediatrics was given by the Royal College of Physicians of London. We understand that this is not so, and it is therefore unnecessary to address further inquiries to the College.

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