sound basis, has recently developed (in collaboration with Rayner-Keeler of New Bond Street) a modification of the old Bailliart instrument which should increase the accuracy and enhance the usefulness of this procedure.

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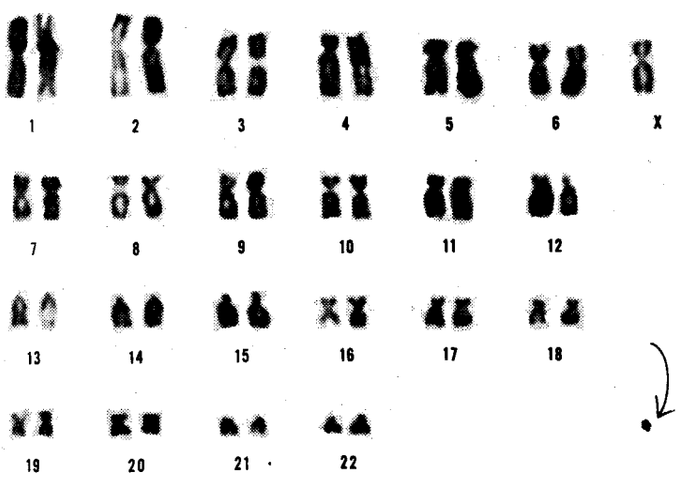
GONADAL DYSPLASIA AND ENLARGED PHALLUS IN A GIRL WITH 45 CHROMOSOMES PLUS "FRAGMENT"

SIR,—A $4^1/_2$-year-old girl was referred to this unit for investigation of growth failure, developmental retardation, and enlarged clitoris.

Her birthweight was 6 lb. 6 oz., but at twelve months she weighed only 10 lb. The serum-protein-bound-iodine was then 5·6 μg. per 100 ml. and the urinary 17-ketosteroid excretion was 0·63 mg. over an 18-hr. period. The bone-age was 8 months. She first sat without support at sixteen months, walked at thirty months, and talked at forty months. Her parents and her 3 siblings were healthy and of above average size.

Her growth and development were obviously retarded. She weighed 23 lb. (10·4 kg.) and was $33^3/_4$ in. (85·7 cm.) tall. Her blood-pressure was 110/80 mm. Hg. Her hair was coarse, thick, and straight, with a low cervical hair-line. She was moderately hirsute, but had no axillary or pubic hair. Her ears were set low, and her palpebral fissures sloped laterally downwards, in contrast to a mongol. There was an internal strabismus of the right eye. Her mandible was hypoplastic. No abnormalities were detected in the heart or chest; and abdominal examination was negative. The clitoris was enlarged: it was 2·0 cm. long. There were no palpable masses in the labia, but they were partly fused posteriorly. The femoral pulses were strong. The gait was stiff and awkward, and the feet were in extreme pronation. Movements of the hands were clumsy, and a coarse rhythmic tremor of the right arm appeared when the child became upset.

No peripheral chromatin was seen in the nuclei of the buccal epithelial cells. Chromosome studies, by the peripheral-leukocyte-culture method of Moorhead et al.,[1] revealed 45 chromosomes and an additional small piece of chromatin. This piece was observed in all the cells technically suitable for chromosome counting. Karyotypes were prepared from enlarged photomicrographs. There appeared to be a normal complement of autosomes and only one X chromosome. The small piece of chromatin, approximately one-half the length of a number 22 chromosome, was elongated, but had no visible centromere (see figure). The relative length of this "fragment" was 1·0–1·1% of the total X-containing haploid set, and remained constant in all cells which were studied, although the absolute lengths varied with the degree of contraction of the chromosomes in different cells.



Karyotype with 45 chromosomes plus "fragment".

1. Moorhead, P. S., Nowell, P. C., Mellman, W. J., Batipps, D. M., Hungerford, D. A. *Exp. Cell Res.* 1960, **20**, 613.

The findings in this child are similar to those in patients with gonadal dysplasia and phallic enlargement, described by Wilkins.[2] The patients all lacked peripheral chromatin in their buccal epithelial cells, and were found to have either nests of Leydig cells in the primitive gonadal streaks or rudimentary intra-abdominal testes. Although we have not yet established this in our patient by direct inspection or biopsy, it seems possible that she also has some testicular elements in her dysplastic gonads. The additional piece of chromatin may represent a portion of the Y chromosome.

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ASSOCIATION OF ACROCENTRIC CHROMOSOMES WITH THE CENTROMERE REGION OF CHROMOSOME NO. 1

SIR,—The article by Dr. Ferguson-Smith and Mr. Handmaker (March 25) on the satellited human chromosomes prompts me to report another observation of non-random autosomal association in dividing somatic cells. More frequently than would be expected by chance I have seen a large or small acrocentric chromosome (Denver no. 13, 14, 15, 21, or 22) adjacent to chromosome no. 1, usually at right-angles, with the satellited end pointing towards the centromere of no. 1.

I have observed this more often in squash preparations from short-term leucocyte cultures than in coverslip preparations from fibroblast-like monolayer cultures. I noted the association particularly in cells in which the satellites are prominent on several of the acrocentrics elsewhere in the cell, and where the chromosomes are long and the chromatids are parallel, rather than exhibiting chromatid repulsion and flaring of the arms in an "X" configuration. It also appears more often in cells where other satellited chromosomes are found to be associated as described by Ferguson-Smith and Handmaker.

In the accompanying table are set out the results of analysing 66 cells selected because both no. 1 chromosomes and any closely adjacent chromosome could be identified. In most cases, all the chromosomes in the complement could be accurately grouped. These cells were derived from normal females (XX), thereby eliminating any confusion of the Y chromosome with no. 21 or 22. In approximately 24% of the cells chromosome no. 1 was associated with 13, 14, 15, 21, or 22, compared with 6% of cells in which this association was with 16, 17, 18, 19, or 20, which were taken as controls. The association of acrocentrics with each other was observed in 73% of the cells.

ASSOCIATION OF NO. 1 CHROMOSOMES WITH ACROCENTRIC AND METACENTRIC CHROMOSOMES

Culture	Number of cells	No. 1 with 13, 14, 15, 21, or 22	No. 1 with 16, 17, 18, 19, or 20	Satellite association
Leucocyte	32	10 (*31%*)	1 (3%)	20 (*63%*)
Fibroblast	34	6 (*18%*)	3 (*9%*)	28 (*82%*)
Total	66	16 (*24%*)	4 (*6%*)	48 (*73%*)

If this casual observation is not spurious and if it is confirmed by other cytologists, several hypotheses may be considered. First, it has been suggested that the acrocentric satellited autosomes are "sticky", and that when the cell is squashed, the likelihood that they will be "caught" against a large chromosome is greater than the chance that they will remain isolated or pushed against a smaller chromosome. Secondly, it is conceivable that non-random association is the rule among all chromosomes of the cell and these observations mark the

2. Wilkins, L. The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence; p. 269. Springfield, Ill., 1960.

beginning of a detailed orderly spatial grouping of the entire chromosome set before metaphase. Corroborative evidence for such a pattern might be the paranuclear positioning of the sex-chromatin body at interphase. Alternatively, it may be due to non-random positioning of the centromeres on the spindle. In the latter case, one would expect to observe a more frequent association in unsquashed cells not treated with colchicine in which the spindle is not distorted or destroyed.

Finally, these observations call for a re-evaluation of the " nucleolar chromosome " first described by Schultz and St. Lawrence [1] in the pachytene stage of human spermatogenesis. Unfortunately, these investigators were unable to identify the entire chromosome complement because of " possible associations of the heterochromatic regions of non-homologous chromosome pairs ". Furthermore, they could not identify the centromere regions in their preparations, but they described the nucleolar chromosome as being one of the longest chromosomes, with approximately equal arms on either side of the nucleolar-organising region. They did not entirely rule out the possibility that the two " arms " on either side of the nucleolus might be two chromosomes in end-to-end association. This latter interpretation is consistent with the observations of Ferguson-Smith and Handmaker. However, Schultz and St. Lawrence favoured the view that the nucleolar chromosome was, in fact, a single two-armed chromosome. If they are correct, and if their chromosome is in fact no. 1, then the association of chromosome no. 1 with an acrocentric chromosome is to be expected in view of the general agreement that the short arms of the satellited acrocentrics are heterochromatic and concerned with nucleolar organisation. This would suggest, then, that the paracentric region of no. 1 also contains a nucleolar-organising region. Further data are needed to clarify the issues raised.

I should like to thank Mrs. Phyllis Rabbideau and Miss Freda Nishimura for their technical assistance.

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SALICYLHYDROXAMIC ACID IN TREATMENT OF SCALP MYCOSES IN CHILDREN

SIR,—Salicylhydroxamic acid is a new and promising method of treating scalp mycoses without epilation with X rays. It inhibits the growth of fungi,[2 3] and clinical trials have been reported.[3 4]

We used this compound against endothrix, ectothrix, and endoectothrix, both orally (1–2 g. a day) and superficially with ointment. Treatment lasted for from 15 to 39 days; and we treated 53 cases in all. Only 2 cases failed to respond despite treatment prolonged to 95–100 days: the fungus seemed completely resistant in them.

To 12 of the 29 children with endothrix the drug was given orally only; and 8 were clinically healed after less than 30 days, and 1 after 52 days. In 3 particularly severe cases treatment had to be continued for more than 60 days. Recession of the fungus was noted microscopically after 7–27 days of oral treatment.

The other 17 children were initially treated orally; and then, after suppuration had been controlled, salicylhydroxamic acid was also applied externally as a 5% ointment in ' Vaseline '. In 10 of these cases clinical cure was obtained after 15–30 days, in 6 after 30–40 days, and in 1 after 62 days.

In only 1 child with endothrix was fungus present at the third examination $3^1/_2$ months after he left hospital. This we regard as the only failure, although it might be due to reinfection.

24 children were infected with ectothrix. We applied 5% ointment only (twice a day) in 7 mild cases with one or two fungal patches of 2–3 cm. diameter. All were cured within 17–47 days. But 1 case relapsed, after 20 days of treatment, on the 36th day after leaving hospital.

In the other 17 cases (widely disseminated scalp mycosis) both oral and topical treatment was given. A permanent cure was achieved in 8. The clinical signs abated after 15–54 days, and microscopical examination was negative after 10–17 days. No growth of fungus on synthetic medium could be obtained after 12–33 days.

Out of a total of 24 cases of ectothrix, we recorded 14 cures, 7 relapses, and 3 probable reinfections.

The patients with endothrix were examined at least three times during the 2–6 months after leaving hospital. Only scars were observed, and no inflammation of the skin and no fungus.

The patients with superficial mycoses were observed for 3–12 months.

We conclude from our 2 years' experience that salicylhydroxamic acid seems useful in treating children with mycoses of the scalp.

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A PHYSICAL SIGN OF HÆMOPERITONEUM

SIR,—The early signs of hæmoperitoneum are often hidden by those produced by superficial injuries such as fractured ribs or contusion of abdominal muscles. Localised guarding and tenderness is found over an area of abdominal-wall injury as well as over an area of hæmoperitoneum.

Shoulder-tip pain (Kehr's sign) may be due to a tear in the diaphragm or to irritation of its surface by blood. It is present in only about 12% of patients with ruptured spleens. Seagesser's phrenic point test is equally non-specific. Rupture of a solid viscus becomes more easily distinguishable from parietal injury when a large quantity of blood has accumulated in the peritoneal cavity, because of the rising pulse-rate, the deepening or reappearance of shock, the increase in the extent of abdominal guarding and tenderness, or the appearance of a mass. Ballance's sign of fixed dullness in the left flank associated with shifting dullness in the right flank will only be present after a considerable amount of blood has been lost from the circulation after rupture of the spleen.

In the early stage, after injury, the delay in pain reaction peculiar to hæmoperitoneum has been found most helpful. When the abdomen is firmly palpated, as when testing for " deep tenderness ", this tenderness and muscular rigidity can be shown to appear after an interval of about half a second. This delay can be very clearly demonstrated by asking the patient to turn on one side. Unless abdominal-wall trauma is extensive the patient will begin to turn with little pain, but is suddenly gripped by severe pain when he is about halfway on his side, and then either rolls back to his original position or drops on his side in obvious pain. This turning test can only be demonstrated once or twice as the patient quickly learns what to expect.

I have been able to demonstrate this sign in the 7 patients with ruptured spleens and 2 with ruptured livers I have seen in recent years. It was most helpful in establishing an early diagnosis. 1 patient with rupture of both spleen and liver was too ill to turn on his side. Diagnosis was, however, obvious from the delayed reaction to palpation. The sign was present in a boy of $2^1/_2$ whose ruptured Meckel's diverticulum had bled into the peritoneal cavity as well as into the lumen of the ileum. It was present in 2 patients with ruptured tubal gestation but absent in others.

The explanation of the phenomenon of delayed pain reaction in hæmoperitoneum may lie in the characteristic response of peritoneum to shed blood. The peritoneum reacts differently to different fluids. Pus and gastrointestinal contents set up an intense inflammation associated with board-like muscular rigidity. The inflammatory response to urine is less severe. Chyle and ascitic fluid produce no inflammation and do not

1. Schultz, J., St. Lawrence, P. *J. Hered.* 1949, **40**, 30.
2. Halweg, H., Krakówka, P. *Bull. Acad. pol. Sci. Cl.* 3, 1955, **3**, 437.
3. Alkiewicz, J., Eckstein, Z., Halweg, H., Krakówka, P., Urbański, T. *Nature, Lond.* 1957, **180**, 1204.
4. Ryll-Nardzewski, Cz. To be published.