NAIL-PATELLA SYNDROME WITH ILIAC HОРNS
AND HEREDITARY NEPHROPATHY
Necropsy Report and Anatomical Dissection

D. DARLINGTON and C. F. HAWKINS, BIRMINGHAM, ENGLAND
From the Departments of Anatomy and Medicine in the University of Birmingham

The nail-patella syndrome, also called hereditary onycho-osteodysplasia, arthro-onycho-
dysplasia and onycho-mesodysplasia, is of interest to clinicians and geneticists because of the
variety of congenital abnormalities. It is easily recognised by the appearance of the
finger nails, which are dystrophic or absent. Thumb nails are most commonly involved,
other nails becoming progressively less affected towards the little finger. Men often show
hemidysplasia of the cubital side of the nail (Montant and Eggermann 1937) whereas women
have a small, apparently normal base with the nail gradually fading away so that the flesh
at the end of the finger turns over the nail. Toe nails are usually normal. The patellae are
often absent or rudimentary. Usually a triad of anomalies is completed by arthrodysplasia
of the elbows (Lester 1936, Senturia and Senturia 1944). A poorly formed and backwardly
subluxated head of the radius articulates with a small underdeveloped capitulum. This
causes an increased carrying angle, reduction of supination and incomplete extension of the
elbow.

Iliac horns are a frequent manifestation of the syndrome (Fig. 1). These bilateral conical
projections arise from the centre of the posterior surfaces of the iliac bones (Kieser 1939;
Fong 1946; Mino, Mino and Livingstone 1948; Thompson, Walker and Weens 1949; Hawkins
and Smith 1950; Wildervanck 1950; Gadekar, Chawla and Anand 1962). Proteinuria may
be present (Kieser 1939). Hawkins and Smith (1950) suggested that this was due to congenital
renal dysplasia and was part of the nail-patella syndrome. This is now accepted (Whalen and
McIntosh 1962).

The death of the propositor of the family described by Hawkins and Smith (1950) provided
an opportunity for detailed dissection of the iliac horns and deformed joints and histological
examination of the kidneys.

CASE REPORT

The patient first attended hospital when he was forty-five, complaining of frequency of
micturition. The nail-patella syndrome was diagnosed and iliac horns were seen on radiographs
taken for intravenous pyelography. He was pale and asthenic, but his health had been
satisfactory and he worked as a manual labourer. He also suffered from vague back pains,
probably originating from the kyphosis. His skin, especially on the trunk, showed many
angiomata between two and six millimetres in diameter, the larger ones being on pedicles,
and there were areas of pigmentation. Hemidysplasia of the outer half of both thumb nails was
present, other nails being normal (Fig. 2). The elbows showed an increased carrying angle;
extension was limited by 10 degrees and pronation by 30 degrees. There was pectus carinatus.
The patellae could not be palpated. Slight prominences from iliac horns could be seen on
each buttock eight centimetres below the superior iliac crest and thirteen centimetres from the
midline. His height was 1.76 metres and weight 63 kilograms. The cardiovascular system was
normal, the blood pressure being 130/80 millimetres of mercury. Abdominal, respiratory and
central nervous systems were also normal. There was persistent proteinuria with two to three
parts of protein per litre of urine (Esbach’s method). Specific gravity of the urine varied
between 1·015 and 1·022; it was sterile, though containing casts of all types with occasional red blood cells and pus cells. The blood urea was persistently raised, usually 60 milligrams per 100 millilitres; serum albumin was 2·9 grammes; and globulin 2·3 grammes per 100 millilitres. The Van Slyke urea-clearance test (MacLean) gave a maximum concentration of 2·1 per cent urea. Intravenous pyelography excluded polycystic disease. The blood count, cerebrospinal fluid and erythrocyte sedimentation rate (Westergren) were then normal. The Wassermann reaction was negative. Radiographs showed the following skeletal changes: arthrodysplasia of both elbow joints; spina bifida at the seventh cervical vertebra, with long transverse processes of the seventh cervical and first sacral vertebrae; rudimentary patellae; and well developed bilateral iliac horns and a small exostosis arising from the right pubic bone.

The patient's condition began to deteriorate about two years before his death. The blood pressure had risen to 200/120 millimetres of mercury and the blood urea gradually increased to 325 milligrams per cent; serum electrolytes were normal except for a terminal rise in potassium to 6·5 milli-equivalents per litre. He died from uraemia at the age of fifty-two.

Necropsy

There was terminal bronchopneumonia and recent fibrinous pericarditis. The heart weighed 550 grammes and showed left ventricular hypertrophy with severe atheroma of the coronary arteries and aorta. The anatomy of the lungs and their fissures, and the heart and blood vessels, was normal. No abnormality was seen in the alimentary tract except for diverticulosis of the colon. Other organs examined and found to be normal were the tongue, pharynx, liver, gall bladder, biliary passages, pancreas, spleen, suprarenal glands, thyroid gland, meninges, brain and spinal cord, bladder, prostate, seminal vesicles and testes. Histological studies were carried out on all these tissues and no abnormality was seen.

The kidneys were both slightly reduced in size, the right weighing 110 grammes and the left 100 grammes. There was a thin-walled cyst 4 centimetres in diameter at the upper pole of the right kidney, and a few smaller cysts, from 0·2 to 0·5 centimetre in diameter in the subcapsular cortex of
both kidneys. The capsules stripped readily, revealing fine granular surfaces, and sections showed marked thinning of the cortex with loss of striation. Each renal pelvis was normal. Microscopy of the kidneys (Dr D. B. Brewer) showed marked increase of interstitial fibrous tissue in the form of dense interconnecting bands, producing a reticular network (Fig. 3). Amongst these fibrous bands were numerous atrophic remnants of tubules, and in the spaces of the network were nodules of hypertrophied and dilated tubules. Many of the glomeruli associated with these tubules showed adhesions, though most adhesions were slight; there was no thickening of glomerular basement membranes. Most glomeruli lying within the bands of fibrosis showed marked atrophy, some being replaced by hyaline nodules; there was also moderate focal lymphocytic infiltration. The smaller arteries showed slight intimal thickening, though without hyperplasia of the internal elastic lamina. There were moderate hypertensive changes in the arterioles and a few showed necrotising arteriolitis.

![Histological appearance of the kidney in hereditary nephropathy. This shows the peculiar reticular distribution of the scarring. (Periodic acid Schiff × 100.)](image)

**FIG. 3**

**DISSECTION**

**Pelvis**—The bony spurs or “horns” projected laterally from the external surface of each iliac bone and were symmetrical (Figs. 4 and 5). Each had a broad base at its attachment, an upper subcutaneous surface and a lower surface subdivided by a rounded lateral border into an anterior and a posterior part. Upper and lower surfaces were separated by anterior and posterior borders which met at the tip of the horn. The horn was attached at approximately the junction of the middle and posterior thirds of the line joining the anterior and posterior superior iliac spines; its broad base filled in the shallow concavity normally found in the posterior half of the gluteal surface of the ilium. Each horn lay opposite the sacro-iliac joint and appeared to be in line with the lateral part of the sacrum.

There were other abnormal features of the ilium. The iliac crest, between its highest point and the anterior superior iliac spine, was straight instead of convex (Fig. 6). The tubercle of the iliac crest was absent so that, from above, the crest again appeared straight instead of showing the normal lateral convexity at this point. The corresponding tilt in the plane of the gluteal surface was also absent, and the anterior superior iliac spines projected forwards and laterally instead of forwards and medially.

The bulk of the gluteus medius muscle had a musculo-tendinous attachment to the anterior and posterior surfaces and tip of the horn (Fig. 7). Tendinous parts were arranged as intramuscular septa extending into the muscle from the thickened and almost tendinous gluteal fascia covering that part of the muscle attached to the tip and anterior surface of the horn. On the right side this fascia was so thick as to comprise a superficial tendon of origin. Anterior to the horn there were two low, though distinct, ridges on the bone equivalent to the anterior (middle) and posterior gluteal lines, where the rest of this muscle was attached. The upper ridge, or posterior gluteal line, was continuous.
with the anterior border of the horn so that anterior and posterior borders of the horn appeared to be part of the posterior gluteal line (Fig. 6).

The origin of the gluteus minimus muscle was normal, apart from an indentation of its upper border caused by the base of the horn. The origin of the gluteus maximus, a muscle which lay entirely posterior to the horn, was also normal except that its upper border fell short of the iliac crest and posterior superior iliac spine (Fig. 8). Here the muscle was attached to the superficial surface of a thin strong fascial sheet, the fibres of which radiated downwards and forwards from the posterior superior iliac spine across a supero-lateral extension of the sacro-tuberosous ligament which arched upwards and laterally to gain additional attachment from the posterior border of the horn. Below, this fascial sheet fused with the fascia covering the gluteus medius. The insertions of the three gluteal muscles were normal.

The only other soft-tissue anomaly was the bilateral extension of the origin of superficial fibres of the vastus lateralis and vastus medialis muscles by means of a fascial band; this passed upwards
and medially across the hip joint to be attached to the ilium, below and lateral to the anterior inferior iliac spine, and to the reflected head of the rectus femoris muscle. Some deeper fibres of these muscles also gained attachment from the ilio-femoral ligament in front of the joint.

The finding of an open sacral canal (Fig. 5) prompted examination of the neural arches of the rest of the vertebral column. A very narrow midline slit was found between the two halves of the neural arch of the seventh cervical vertebra, the spinous process of which was bifid. There was marked asymmetry of the neural arch of the fifth lumbar vertebra. Otherwise the neural arches were normal.

The knees—Both knees were dissected but as the differences between them were negligible, only one is described. The patella was small though otherwise normal; it had a maximum length and width of only 30 millimetres, whereas the normal patella has a length and width of approximately 45 millimetres. On the femur a narrow groove interrupted the normal continuity of the surfaces of the femoral condyles (Fig. 9); this extended forwards and upwards from the intercondylar fossa to the anterior surface of the bone. Lodged within the groove was a tendinous band attached below to the front end of the intercondylar fossa and above to the anterior surface of the femur above the medial part of the articular surface of the lateral condyle. At its lower attachment this band formed, in effect, an upper border to the infrapatellar synovial fold.

The infrapatellar synovial fold extended superiorly over the posterior surface of the patella almost in line with the vertical ridge on this surface. At its upper end this fold, ligamentous in structure, was loosely attached to both the anterior surface of the femur and the posterior (deep) surface of the quadriceps femoris muscle. It formed a thickened free lateral border of a membrane which stretched medially, partially subdividing the synovial cavity anterior to the medial femoral condyle into anterior and posterior compartments. The compartments communicated with each other

---

**Fig. 8**
Posterior view of gluteal dissection. The broken lines indicate the upper border of origin of the gluteus maximus muscle. Gluteus medius and gluteus minimus are shown on the left and right sides. The extension of the right sacrotuberous ligament to the horn is also shown.

**Fig. 9**
Figure 9—Anterior view of the lower end of the left femur. The patellar articular surface is interrupted by a groove, which lodges a tendinous band attached to the femur above and below through the infrapatellar synovial fold. Figure 10—Posterior view of the left tibia and the anterior part of the capsule of the knee. The infrapatellar synovial fold extends upwards and medially as an incomplete membrane, subdividing the medial half of the patello-femoral part of the joint.
through two large gaps in the membrane (Fig. 10). There was only a narrow communication between the anterior compartment and the lateral half of the synovial cavity of the joint as the membrane had an almost continuous vertical linear attachment to the deep surface of the quadriceps tendon, the medial border of the patella, and the infrapatellar pad of fat. The anterior compartment extended fifteen millimetres higher than the posterior compartment but it ended below five millimetres above the medial meniscus. Medially the two compartments were more or less coextensive. The posterior compartment was continuous with the joint space between the femur and tibia medial to the cruciate ligaments. It also communicated with the lateral half of the joint through the interval between the infrapatellar fold anteriorly and the femur posteriorly (Fig. 11). This interval was crossed by the tendinous band. There was a lateral alar fold but the medial alar fold was absent. The menisci, cruciate ligaments and capsular ligaments were normal.

The elbows—The left elbow only was dissected. The lower end of the humerus presented a massive trochlea, the anterior surface of which extended higher than normal. Between the well marked lateral margin of the trochlea and the lateral epicondyle was an underdeveloped capitulum (Fig. 12). Although its surface was convex in planes parallel to the plane of the lateral margin of the trochlea, it was slightly concave in planes at right angles to the lateral margin of the trochlea, so that the domed shape of the normal capitulum was completely absent. The medial epicondyle was small in relation to the trochlea.

The olecranon fossa was very small and shallow, and the radial fossa was absent. The coronoid fossa was also small, and lodged within it was a circular nubbin of bone about 10 millimetres in diameter and 5 millimetres thick, lying within the cavity of the joint and only loosely attached to the articular capsule.

The articular cartilage of the trochlea was normal though it extended 10 millimetres on the medial surface of the trochlea. Over the lower two-thirds of the underdeveloped capitulum the cartilage appeared rough and fibrous and was absent in its central part, so that approximately 70 square millimetres of smooth bone surface was exposed.

The upper end of the ulna was normal, apart from the absence of the usual indentation of the medial margin of the trochlear notch, and the disposition of the articular surface for the radius in the radial notch. This surface instead of facing almost directly laterally faced upwards as well, so that the angle between it and the articular surface of the trochlear notch was shallower than normal (Fig. 13).

There was a large, deformed head of the radius, and instead of being circular it was elongated in the antero-posterior diameter. In place of the usual shallow concavity, the upper surface of the head showed a transverse ridge dividing it into a posterior third and an anterior two-thirds (Fig. 14). The anterior part sloped downwards and forwards, making the head wedge-shaped and the antero-medial third of its circumference a narrow border. The radial notch of the ulna was in contact with the under-surface of this narrowed border of the radial head. The articular cartilage over the anterior part of the upper surface of the radial head was roughened and fibrous and deficient medially over an area of almost 100 square millimetres exposing a faintly pitted though otherwise smooth bone surface.

The posterior third of the radial head was knob-like and mostly covered with articular cartilage, though a small pit next to the transverse ridge gave firm attachment to the abnormally thickened postero-lateral part of the articular capsule. The thickened capsule formed a wedge of fibrocortical material between the articular surfaces of humerus and radius. The only part of the head of the radius which articulated directly with the humerus was the antero-medial sector, where the articular cartilage was deficient.

DISCUSSION

Iliac horns or spurs were first described by Kieser (1939), although Doub, quoted by Fong (1946), had seen a case in 1925. Brixey and Burke (1950) pointed out that horns can
be seen in the radiographs of the pelvis in a paper by Turner (1933) where he described the syndrome without noticing the horns. Hawkins and Smith (1950) studied iliac horns in nine patients. They had not been noticed by the patients but could often be felt. They were easily seen in the radiograph of a boy of nine months, and terminal epiphyses were seen on the horns of a girl of fourteen. Iliac horns are usually symmetrical and well shaped, quite unlike

the irregular projections of exostoses; nor do they arise close to any normal epiphysis of the ilium. Radiographs show a well marked trabecular pattern. Iliac horns have only been described in the nail-patella syndrome and do not occur in animals.

The present dissection has provided evidence about soft-tissue structures but it has not explained the cause of iliac horns. There was no evidence that the horn owed its origin to the traction of an abnormal muscle. It seems that the hereditary abnormality expressed itself primarily in the iliac bone, around which the gluteal muscles disposed themselves. This supports evidence that the main architecture of a bone is determined by mechanisms inherent in the primordial bone, and only secondarily by interaction with surrounding structures (Murray 1936). Changes in local musculature would follow if the iliac attachment of the
gluteus medius muscle migrated upwards towards the crest of the ilium during development. A horn or its cartilaginous precursor would then interrupt this ascent, leaving the area of bone above it bare of muscle, as in our case. Such migration of gluteal muscles has been described by Bardeen (1907). Recent work has indicated that the gluteal muscles undergo complex morphological changes which continue to a later stage in foetal life than previously supposed (Puzanová 1961, 1963). The fact that the horn projects laterally and directly in line with the lateral parts of the sacrum suggests that it may be an extension of the costal element of the sacrum. Alternatively, it may be homologous to the spine and acromial processes of the scapulae. Abnormalities of the scapulae have been reported in cases of the nail-patella syndrome (Turner 1933, Lester 1936, Renwick 1956), usually due to developmental deficiencies of the coracoid and acromial processes, and bony spurs have occasionally been seen. The scapulae showed no radiographic abnormality in the present case but they were not dissected.

The horns cause no disability. Indeed, there might perhaps be a slight mechanical advantage to the gluteus muscle by increase of its perpendicular distance from the hip joint. However, the absence of the normal overhang produced by the tubercle of the iliac crest would offset this and the gluteus medius was also relatively deficient in long muscle fibres.

The abnormality of the iliac crest was described by Turner (1933) as "an outward flare of the crest in its posterior half." Jameson, Lawler and Renwick (1956), however, used the phrase "anterior part of iliac crest straightened" to describe the anomaly, a description which accords better with our findings. This is sometimes the only abnormality of the ilium; conversely, iliac horns may be present though the crest is normal. There is no previous report of the tubercle of the crest being absent, probably because the normal tubercle is not readily identifiable on radiographs. Similarly, absence of the normal angulation of the gluteal surface below the tubercle of the crest, which gives the bone a somewhat ape-like appearance, would be difficult to detect without dissection.

The knee—Venable (1940) dissected the knee of a patient with the nail-patella syndrome in which there was a very small patella, and found that the anterior cruciate ligament was absent. Renwick (1956) reported normal cruciate ligaments in two cases in which the knees were opened. Our findings resemble those of Nickerson (1945) who published arthrographs of the knees of two patients with very small patellae; in both of his cases the joints were subdivided by an incomplete median septum into a smaller medial cavity and a larger lateral cavity. The defect in the septum was bounded anteriorly by a sharply curved falciform edge facing the centre of the joint space. A diagram of our dissection (Fig. 11) showing the arrangement of the infrapatellar synovial fold and its attachments as seen in a sagittal section through the middle of the joint, explains Nickerson's lateral arthrographs. Nickerson's vertical arthrographs showed a "mass of tissue" medial to the patella of which the medial part was absent. This "mass of tissue" was probably the membrane attached to the medial part of the patella and separating it from the medial femoral condyle.

The femoro-tibial part of the knee has, in its early development, two cavities separated from each other by a septum of intercondylar mesenchyme in which cruciate ligaments subsequently develop (Haines 1953). Later, these cavities communicate with each other and with the cavity of the patello-femoral joint. Persistence of the septum has long been considered possible (Langer 1929) though reports of any such cases have not been found in the literature. The infrapatellar synovial fold is generally thought to be a remnant of the original median septum. Survival of further elements of the septum and of some of the tissues originally separating the patello-femoral and femoro-tibial joint spaces could explain our findings. Persistence of these elements may be responsible for failure of patellar development. The possibility that dissection of our specimen had produced artificial defects in a complete septum was excluded by following the distribution of a radiopaque liquid which had been injected into one side of the joint just before it was opened.
Recurrent dislocation of the patella may occur in patients with the nail-patella syndrome and be associated with poor development of the lower part of the vastus medialis muscle (Nickerson 1945). In the present case the vastus medialis muscles were normal; so were the femoral condyles, unlike many examples of the syndrome where lateral condyles were hypoplastic and medial condyles were prominent (Duncan and Souter 1963, Duthie and Hecht 1963). Neither our patient nor his affected relatives had complained of any disability of the knees and their function was normal. There was no sign of osteoarthritis of the knee although he was fifty-two and had spent most of his life doing heavy manual labour.

The elbow—Hypoplasia of the capitulum of the humerus, often with some degree of posterior dislocation and elongation of the radius, is a special feature of the nail-patella syndrome. Both defects might be caused independently by the nail-patella gene, or one might follow the other. Renwick’s finding of a hypoplastic capitulum with a radius of normal length provided evidence against elongation and consequent dislocation of the radius being the cause of the hypoplasia of the capitulum. Renwick (1956) concluded that initial hypoplasia of the capitulum followed by dislocation and elongation of the radius was a more likely explanation than that the gene had independent actions upon the humerus and radius, and we agree with him. This postulates that primary lack of a humeral capitulum leads to compensatory overgrowth of the posterior sector of the radial head, with filling in of the normal concavity and the interposition of grossly thickened capsular tissues.

The articulation of the ulna with the lower border of the circumference of the radial head and bevelling of the opposing surfaces suggested incipient elongation of the neck of the radius; the attachment of the wedge of fibrous tissue to the head of the radius was reminiscent of the arrangement of menisci in the knee joint. There is nothing, however, in the development of the normal elbow joint to suggest that this might be a primary rather than a secondary attachment.

OTHER ANOMALIES IN NAIL-PATELLA SYNDROME

Various rare anomalies have been recorded in the nail-patella syndrome (Renwick 1956, Duthie and Hecht 1963). Conical projections from the scapulae (Bates 1954, Ritvo 1955), Madelung’s deformity of the wrist joints, and changes in the femoral necks and feet have been reported. Soft tissue may be abnormal and a curious web formation between arms and trunk (Kieser 1939), or alterations in elastic tissues (Gibbs, Berczeller and Hyman 1964) may occur. The lunules of finger nails may be triangular. Widening and darkening of the ectodermal element of the iris of the eye was described by Lester (1936), causing an irregular, wide and dark pupillary border (Caffey 1961).

HEREDITARY NEPHROPATHY

The nail-patella syndrome is one cause of hereditary nephropathy (Hawkins and Smith 1950, Whalen and McIntosh 1962) and whether it differs from other types is unknown. Proteinuria, at first without casts or other microscopic abnormalities, is present from infancy and does not disturb growth. It is also compatible with normal health in adult life without rise in blood pressure or impairment of renal function. Death from uraemia, with a clinical picture identical with terminal nephritis, may occur in middle age though the proteinuria does not prevent some persons living to older ages. The “burnt-out” appearance of the kidneys at necropsy is also similar to that of chronic nephritis.

It is interesting that four members of this family, though unaffected by the nail-patella abnormality, suffered from congenital cataract; this is a component of Alport’s syndrome, the main lesions being hereditary nephropathy and deafness. The initial renal defect in hereditary nephropathy is probably biochemical, for the appearance of the kidney seen by renal biopsy in children of two years with Alport’s syndrome was normal, despite abnormalities in the urine (Castleman and Kibbee 1957, Ohlsson 1963).
ORIGIN OF NAIL-PATELLA SYNDROME

The nail-patella syndrome pleases geneticists, for it is obvious at birth, diagnosed without laboratory aid, and there is no reduction of fertility, and expectancy of life is often normal. It is inherited by a regular autosomal dominant gene, closely linked with the ABO blood group locus (Renwick and Lawler 1955; Jameson et al. 1956; Renwick 1957; Lawler, Renwick, Hauge, Mosbech and Wildervanck 1958). The cause of the widespread involvement of such different tissues is unexplained. It is possible that the genetic influence is exerted at a particular stage of embryological development, affecting bones, ectodermal structures and kidneys in a characteristic manner; or damage to various organs might be due to a specific toxin as in galactosaemia, resulting from an inherited enzymatic defect.

SUMMARY

1. Necropsy and dissection findings of a man of fifty-two who died from nail-patella syndrome are recorded.
2. The significance of the iliac horns are discussed and the literature concerning their development is reviewed.
3. Other anomalies are reviewed and the incidence of hereditary nephropathy is discussed.
4. The genetic origin of the syndrome is outlined but the involvement of such varying tissues remains unexplained.

REFERENCES


