TOXOPLASMOSIS

INTRODUCTION

Toxoplasmosis gondii is an intracellular parasite with multiple animal and avian hosts. Antibodies to toxoplasmosis gondii varies in women of childbearing age between 3.3% in Denver, Colorado to 30% in Los Angeles, California. Other countries report prevalences from 2% in India to 80% in France[1,2]. The incidence of toxoplasmosis is declining in the United States because of public awareness of the danger of infection from exposure to infected cat feces, as well as the freezing of meat prior to sale[3].

The frequency of congenital toxoplasmosis in the United States is not known with certainty, but is estimated at between 400 and 4,000 cases per year[4].

There are three clonal lineages of toxoplasmosis (genotype I, II, and III) that predominate in the United States and Europe. In France, toxoplasmosis genotype Type II accounts for > 90% of human infections. Atypical genotypes have been detected in South America with a higher virulence, resulting in severe congenital infections even with 3rd trimester exposure[5].

T gondii is spread to humans through the ingestion of oocyte contaminated food or water. It invades multiple internal organs and remains dormant. Reactivation then occurs when the host is immuno-compromised. A pregnant woman with activated toxoplasmosis can transmit the organism to her fetus.

Acute toxoplasmosis is asymptomatic in 90% of adults. Symptoms of toxoplasmosis include head and neck non-tender lymphadenopathy, muscle aches, and flu-like symptoms. In immunosuppressed individuals, toxoplasmosis may give rise to pneumonia, hepatitis or myocarditis.

Congenital toxoplasmosis may have significant sequelae that includes blindness, learning disabilities and epilepsy. Long-term follow up is required in order to appropriately assess the sequelae of congenital toxoplasmosis. For example, only 39% of cases of chorioretinitis are diagnosed at birth; 85% by 5 years of age; and 96% before 10 years[6].

DIAGNOSIS - MATERNAL

Serologic testing is required to diagnose acute toxoplasmosis. During an acute infection, toxoplasmosis-specific IgG and IgM rise in 1-2 weeks. Toxoplasmosis-specific IgG peaks at about 2 months after infection. While the IgG level then gradually declines, it remains positive for years. High avidity IgG antibodies to toxoplasmosis exclude the mother from having acquired the infection in the last 3-4 months[7]. A seronegative woman should have a repeat titer in 3-6 weeks. A diagnosis is confirmed if seroconversion occurs. High levels of toxoplasmosis-specific IgM several years after infection are rare[8]. Hence, high titers of toxoplasmosis-specific IgM suggests acute infection. A marked elevation of specific IgG in the presence of specific IgM is also considered diagnostic[9]. False positive results hamper the interpretation of IgM antibody testing[7].

IgA specific antibodies are present in > 95% of acute toxoplasmosis infections. They are detected by 4 weeks after infection and lasts up to 7 months. The presence of toxoplasmosis-specific IgA is, therefore, also diagnostic of an acute infection[9].

Fetal infection rates and severity varies based upon gestational age at infection, the genotype of toxoplasmosis, host genetic predisposition, and host immune status[5].
The likelihood of fetal infection increases from 1% at less than 6 weeks' gestation to > 60% after 36 weeks' gestation[10].
The American College of Obstetricians and Gynecologists recommends screening only high-risk pregnant women or women with fetal sonographic findings suggesting a congenital infection[11]. In France, mothers who are seronegative at the beginning of pregnancy have monthly serologic testing[6].

DIAGNOSIS - FETAL

1st trimester chorionic villus sampling will provide information on placental infection. However, this does not necessarily indicate fetal infection.
In the 2nd trimester evidence for direct fetal exposure can be obtained 4-5 weeks after maternal infection by polymerase chain reaction (PCR) DNA amplification of an amniotic fluid sample. PCR has successfully identified congenital toxoplasmosis infection in 83.3%[10] to 100%[12] of cases. In 2002, real-time PCR that is more reliable and detects smaller amounts of toxoplasmosis became available[6]. The sensitivity is further increased by converting from the B1 gene repeated approximately 30 times to a newer sequence that is repeated 200-300 times[13].

PRENATAL ULTRASOUND

Sonographic findings associated with toxoplasmosis may affect multiple organ systems (Table I; Fig 1-8). However, the sonographic stigmata are not specific to toxoplasmosis alone. Central nervous system involvement is the most common and may have many manifestations. Ventriculomegaly is due to white matter necrosis. The evolution of ventriculomegaly may be quite rapid. Diffuse cerebral involvement and damage can result without ventriculomegaly[14]. The in utero diagnosis of microcephaly occurs less commonly with toxoplasmosis than with congenital cytomegalovirus[15]. A vasculitis in the thalamus and basal ganglia gives rise to lenticulostriate linear echogenicities.

TABLE I. SONOGRAPHIC FINDINGS ASSOCIATED WITH CONGENITAL TOXOPLASMOSIS.

- Ventriculomegaly
- Calcifications
  - Intracerebral
  - Periventricular
  - Retinal
  - Lenticulostriate
  - Myocardial
  - Hepatic
- Cataracts
- Microphthalmia
- Microcephaly
- Non-immune hydrops
- Ascites
- Pleural effusion

- Pericardial effusion
- Hepatosplenomegaly
- Placentomegaly

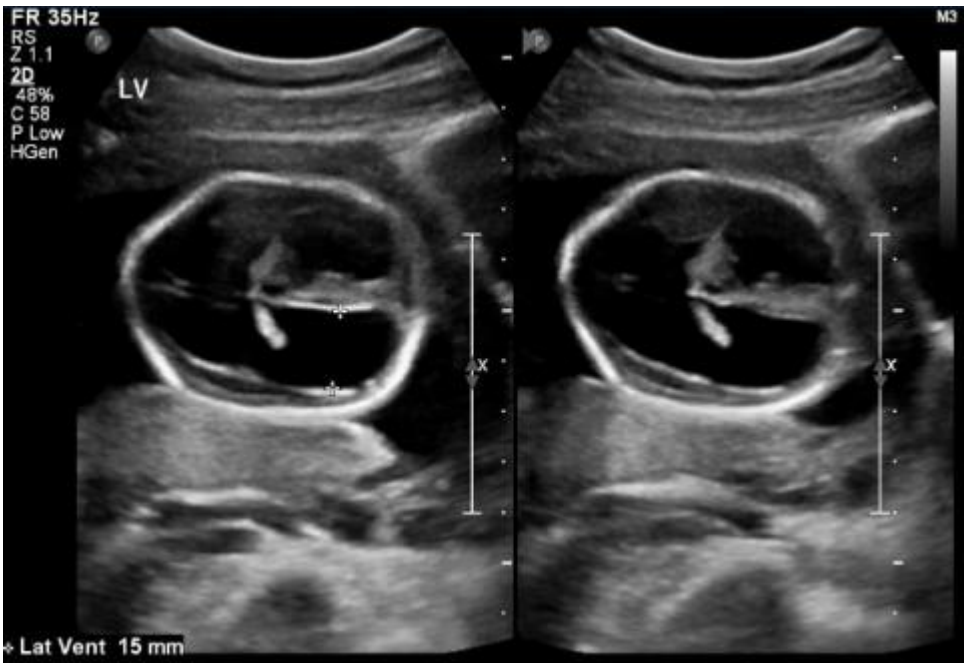

Fig 1. Severe ventriculomegaly. Click for larger image.

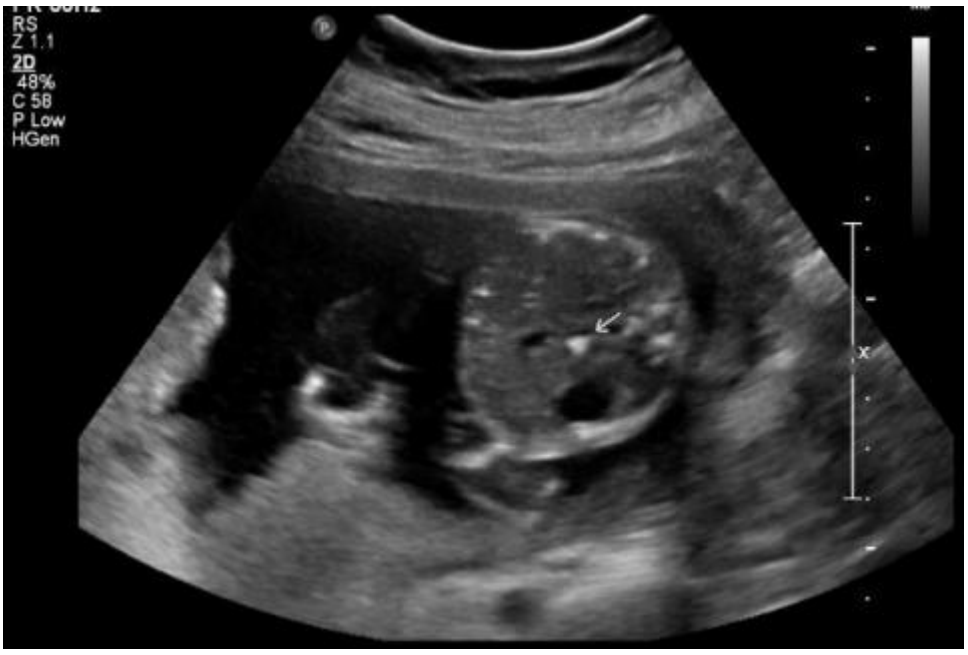

Fig 2. Hepatic calcifications. Click for larger image.

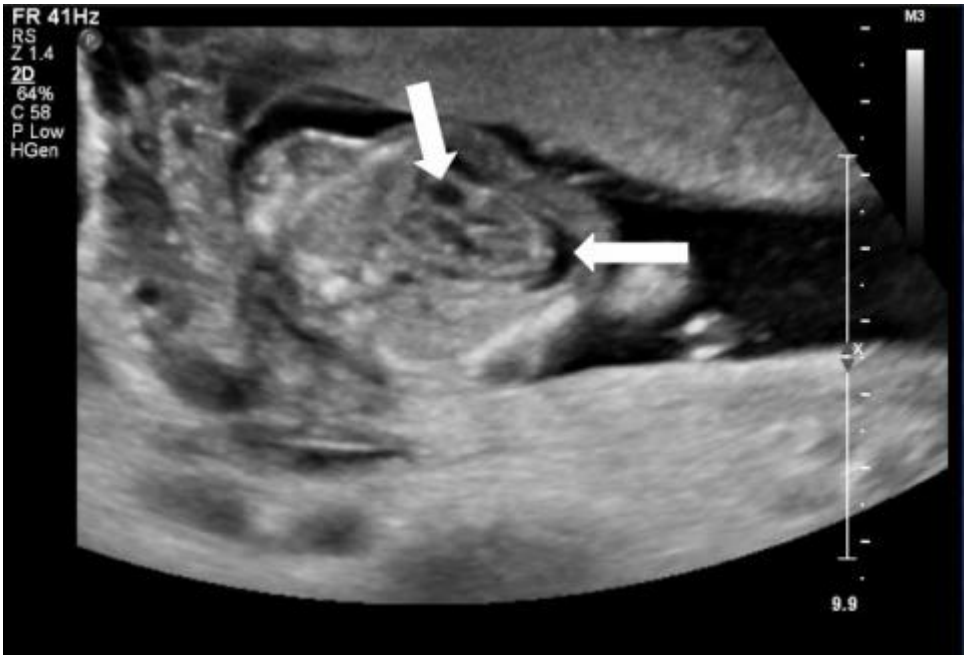

Fig 3. Cardiomegaly and pericardial effusion. Click for larger image.

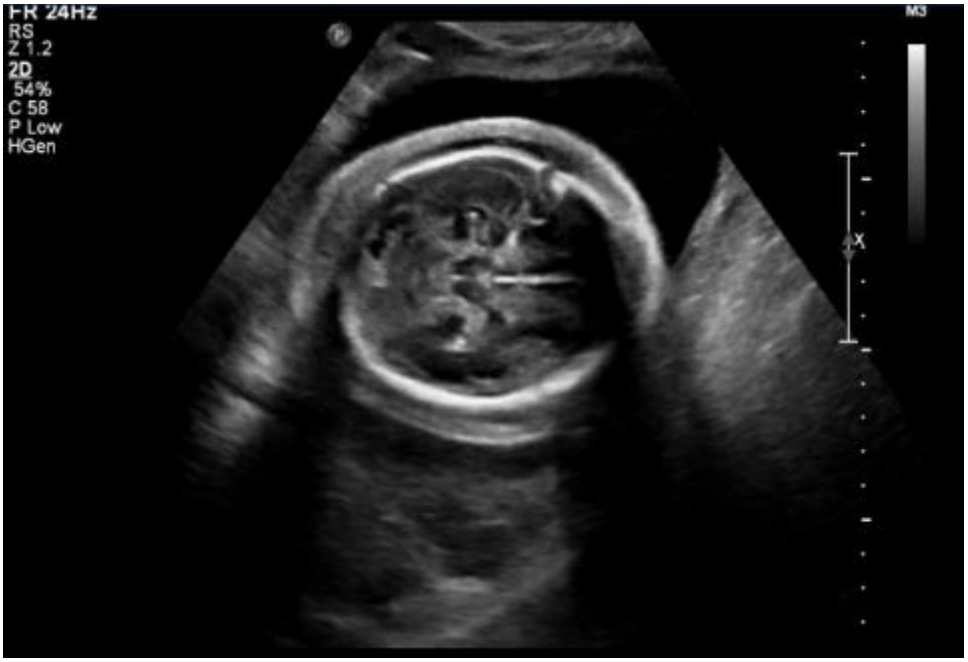

Fig 4. Scalp edema secondary to non-immune hydrops from congenital toxoplasmosis. Click for larger image.

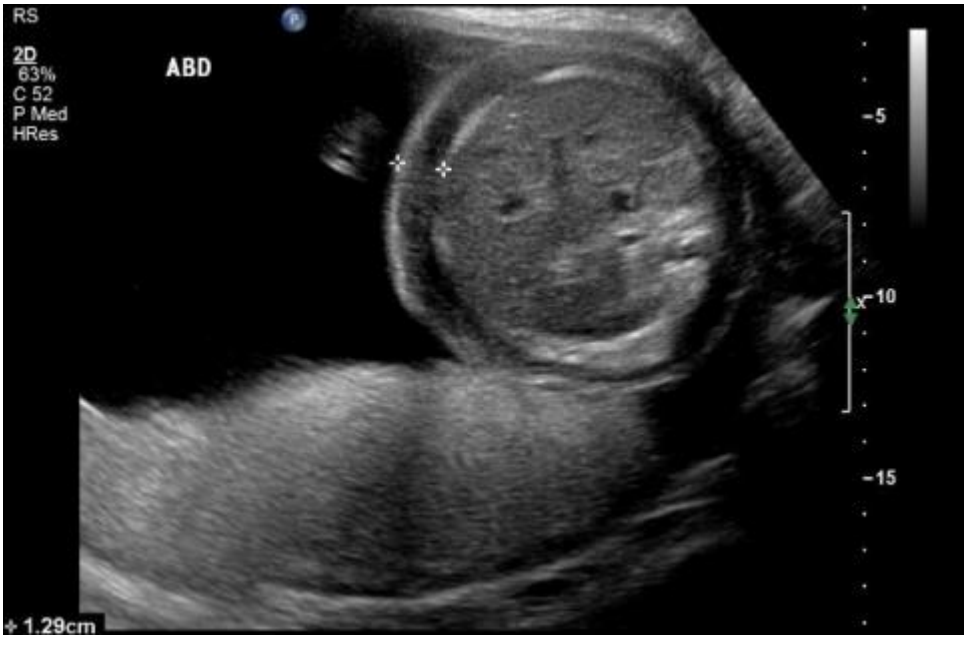

Fig 5. Anasarca (markers). Click for larger image.

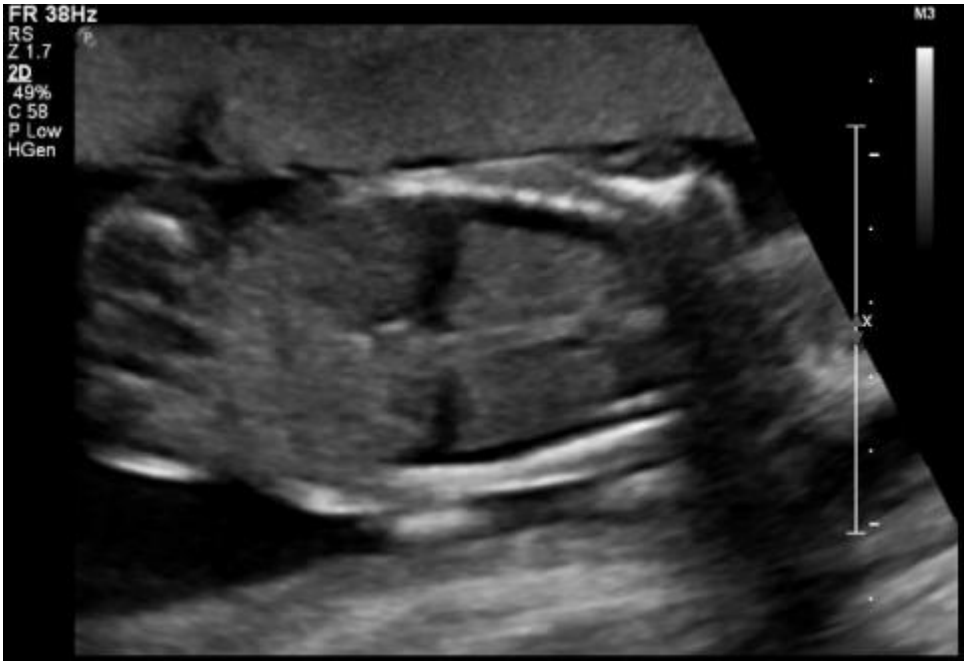

Fig 6. Bilateral pleural effusions. Click for larger image.

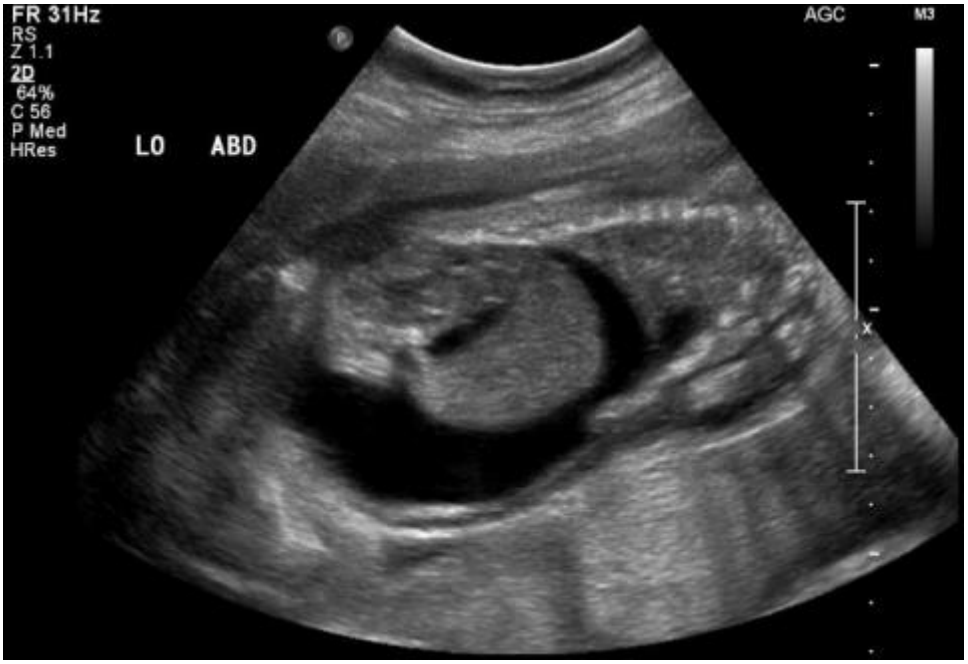

Fig 7. Ascites. Click for larger image.

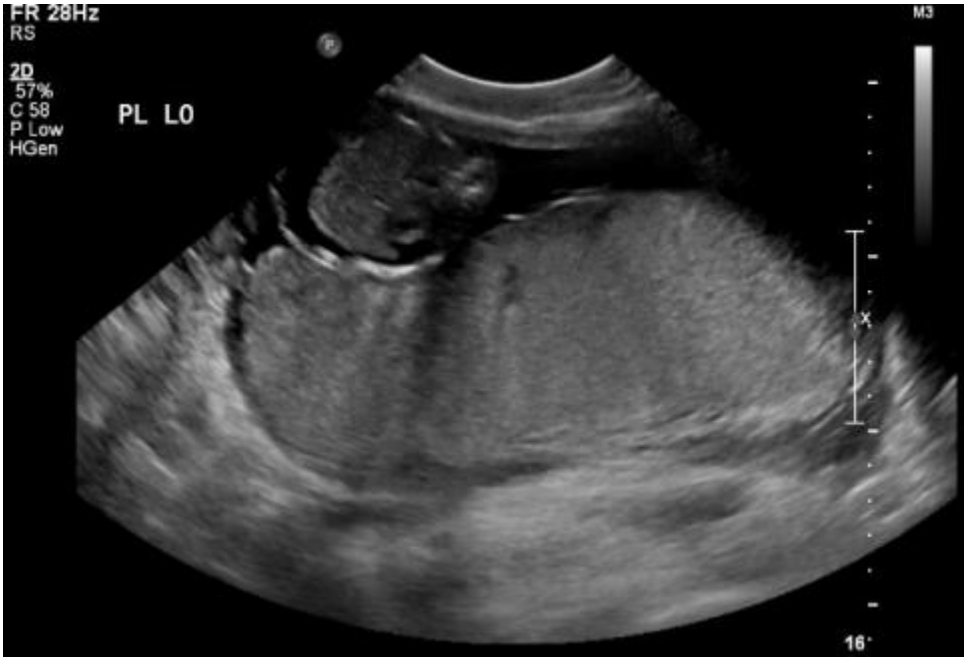

Fig 8. Placentomegaly. Click for larger image.

Cerebral punctate calcifications may be scattered throughout the brain. Rounded periventricular calcifications generally develop with a maternal infection between 20-30 weeks' gestation. A limited number of intracerebral calcifications may spontaneously resolve[16] or resolve with neonatal treatment[14]. The classic sonographic dyad suggesting congenital toxoplasmosis includes ventriculomegaly and intracranial calcifications.

A hemolytic anemia can result in any and all of the manifestations of non-immune hydrops.

Several large studies with excellent results initiated maternal therapy at diagnosis, thereby altering, not only the sonographic detection rate, but also the prognosis of congenital toxoplasmosis when sonographic markers are identified. Hohlfeld and co-workers[14] evaluated 89 fetuses with documented toxoplasmosis. 77.9% and 20.4% of fetuses exposed in the 1st and 2nd trimesters respectively, had sonographic markers associated with toxoplasmosis. More importantly, 54 pregnancies without sonographic findings progressed to term; all of the fetuses had benign toxoplasmosis with normal psychomotor development for up to 4 years. The 89 subjects in this series were reported twice - once to evaluate the songraphic signs associated with toxoplasmosis[14] and again to evaluate infant follow up after in utero treatment[17]. Berrebi and co-workers[18] studies 36 children with congenital toxoplasmosis in the 1st trimester with serially normal ultrasound examinations until birth. As soon as seroconversion was documented, the mothers were treated with spiramycin until delivery. One child (3%) developed severe congenital toxoplasmosis, 19% had chorioretinitis, and 78% presented with subclinical toxoplasmosis. The reliability of ultrasound in detecting fetal toxoplasmosis in a population that does not receive in-utero treatment cannot be extrapolated from the latter reports.

Crino[15] combined 5 studies to obtain a sensitivity of 40%, specificity of 99%, positive predictive value of 98%, and a negative predictive value of 89%. In the United States, if pregnancy termination for congenital toxoplasmosis is a consideration, the detection of sonographic findings prior to 24 weeks' gestation would be required. With a minimum 5 week infection period for the development of sonographic markers, congenital exposure up to 18 weeks' gestation can be assessed.

TREATMENT

Both prenatal and neonatal treatment have been shown to stop the progressive damage from toxoplasmosis and improve outcome[19,20]. The sooner after infection that antibiotics were given to the mother, the less frequent were neonatal sequelae. However, the transmission rate from mother to fetus is not affected by maternal therapy[20].

After documented maternal seroconversion spiramycin (9 million units/day) is prescribed until delivery. If amniotic fluid PCR is positive, or if maternal infection occurs after 32 weeks' gestation, treatment with pyrimethamine (25-50 mg/day), sulfadiazine (3 g/day), and folinic acid twice weekly is prescribed. The latter regimen is administered for 3 weeks, alternating with 3 weeks of 3g of spiramycin daily[20,21]. Neonatal therapy is continued for approximately one year[22].

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